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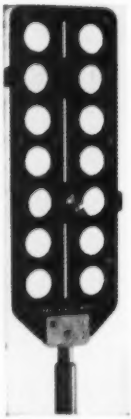

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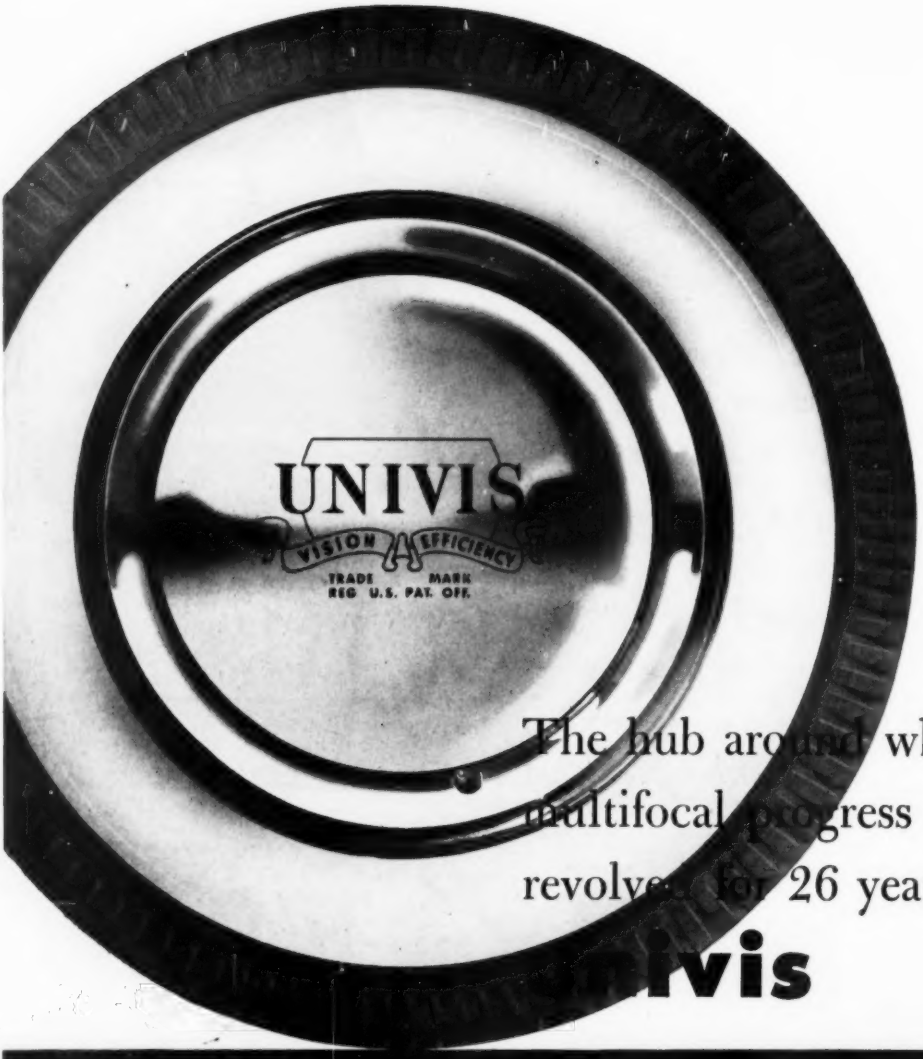

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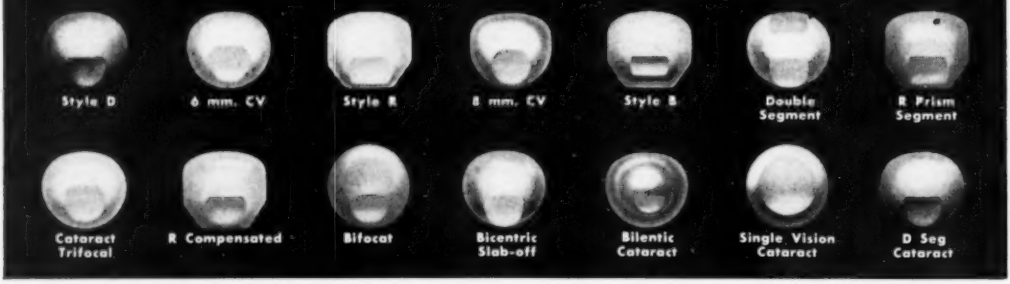

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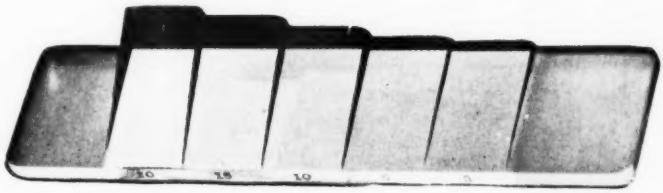

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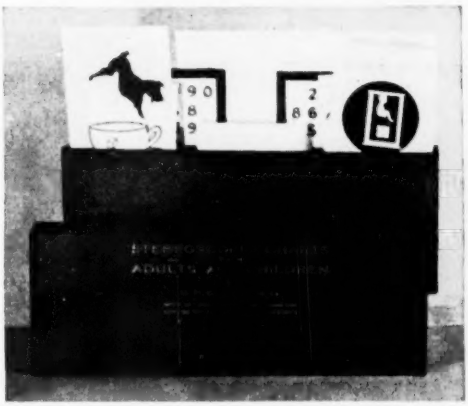

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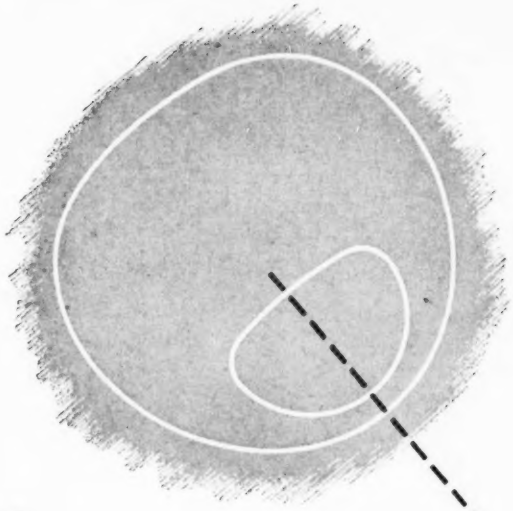

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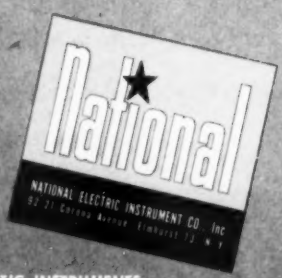

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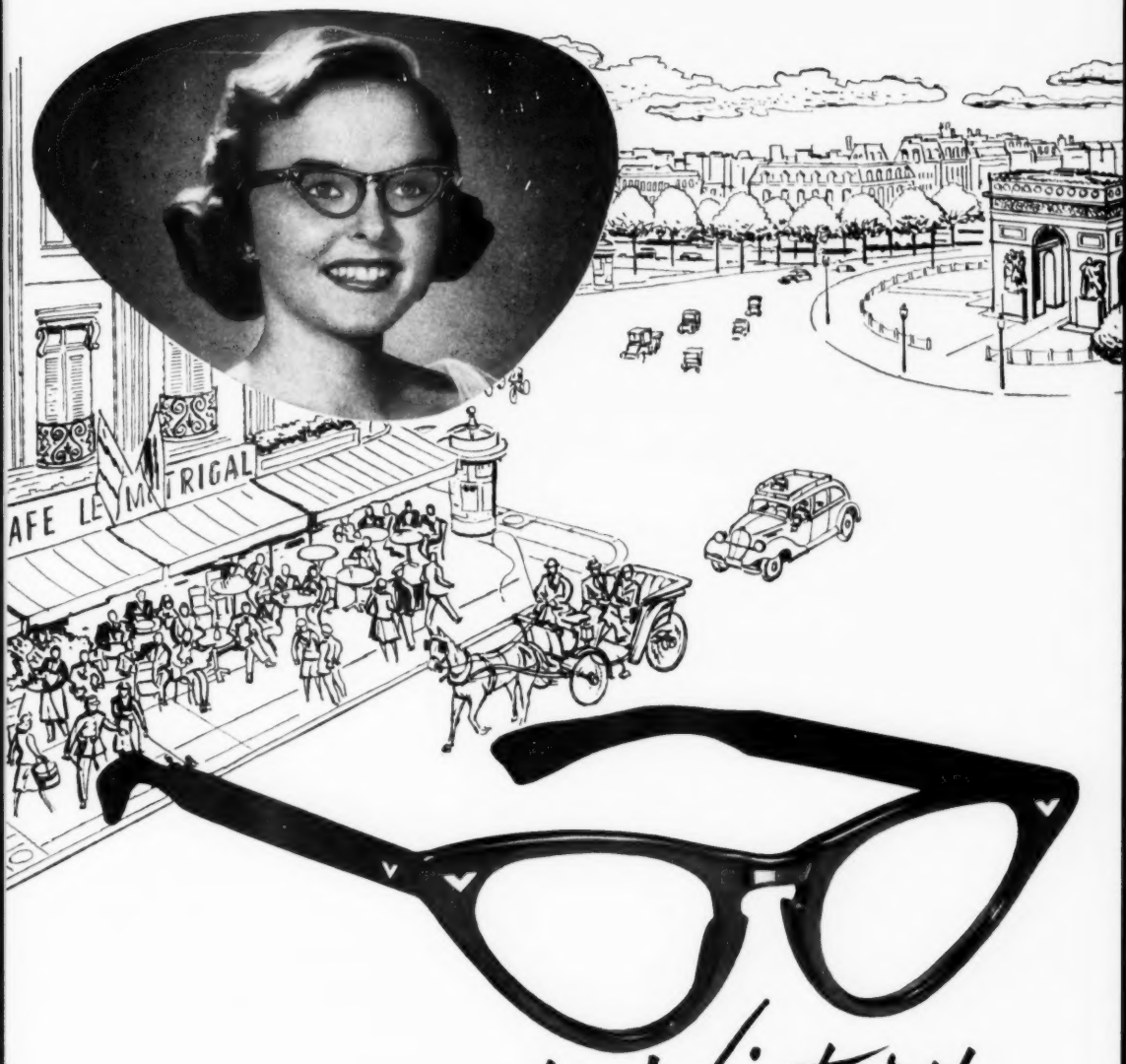

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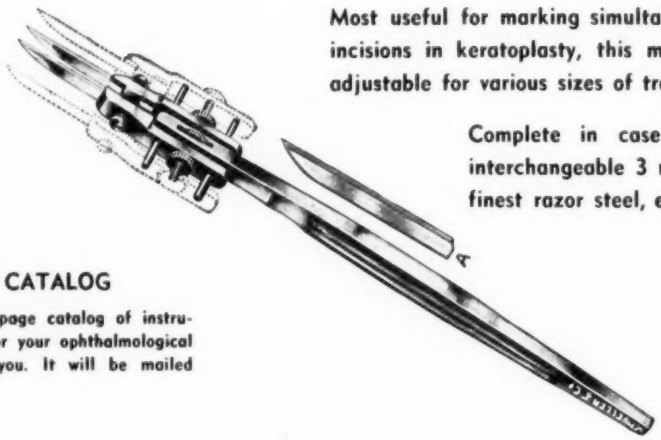

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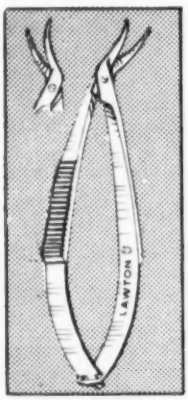

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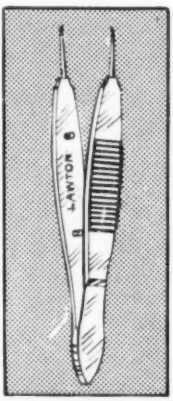

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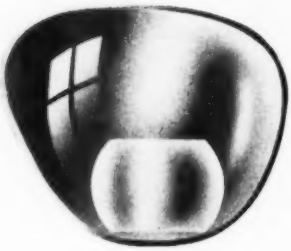

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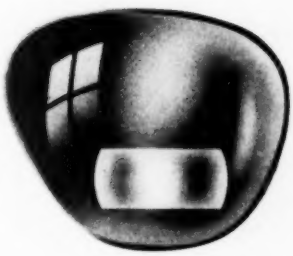

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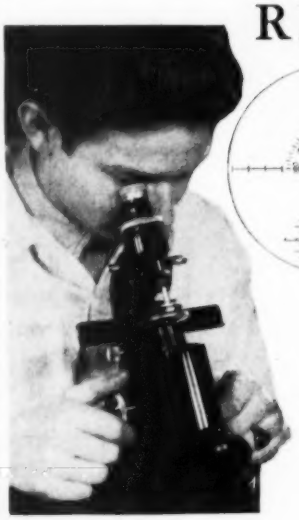

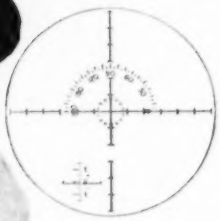

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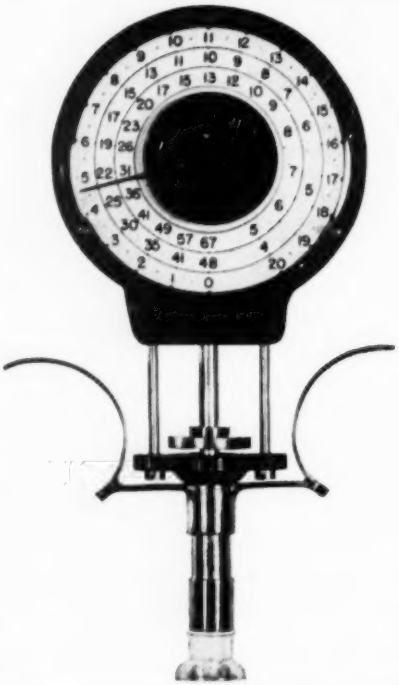

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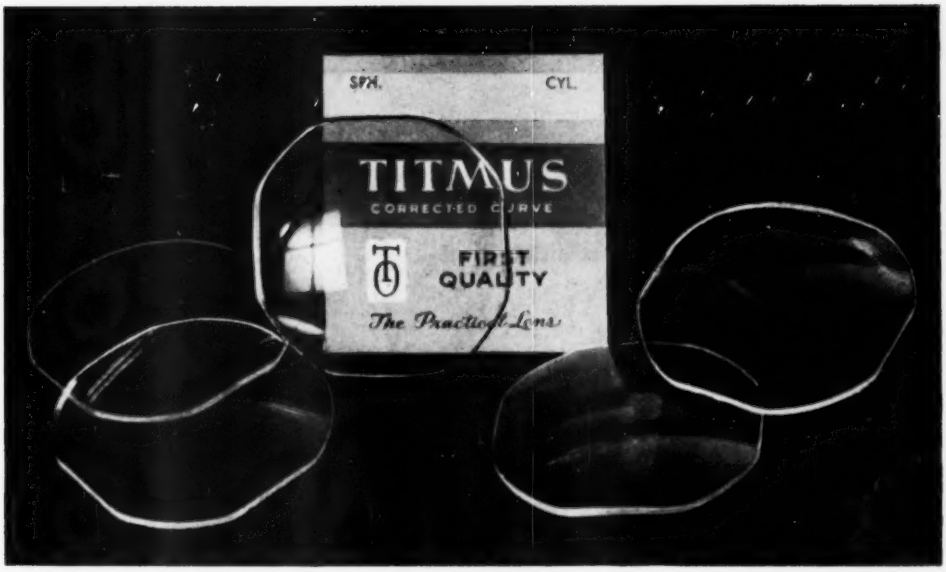

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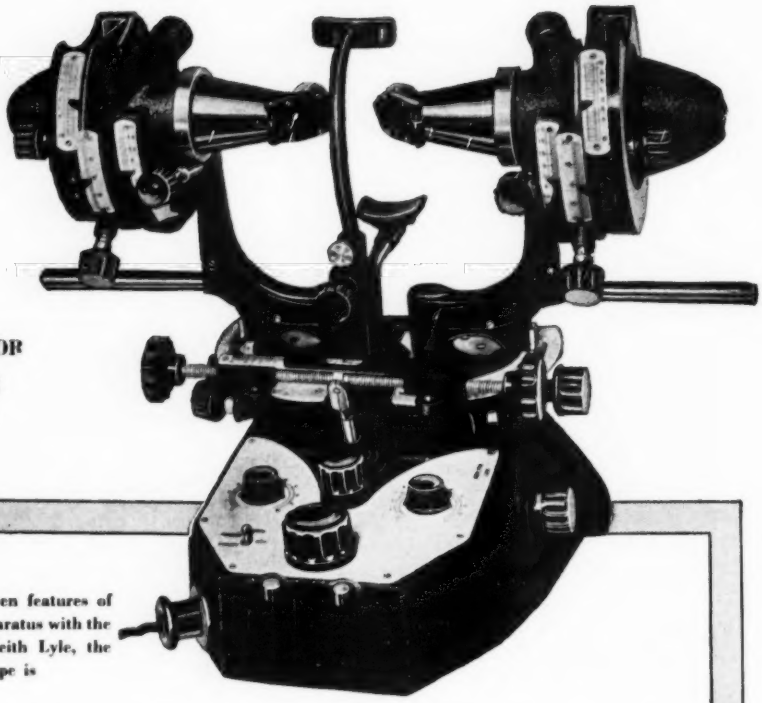

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ELECTRORETINOGRAPHY AND ITS CLINICAL APPLICATION

HERMANN M. BURIAN, M.D.
IOWA CITY

WHENEVER a light stimulus is thrown upon a functioning retina, a typical, reproducible action current can be obtained. Until recently the electric responses of the retina to light stimulation have been used almost exclusively as a tool for the study of retinal physiology in animals. Improved methods of derivation of retinal action currents and other methodologic improvements have made it possible to extend this study also to the human electroretinogram. In the past few years this method of investigating retinal function has gained increasing attention among ophthalmologists in the hope that it may contribute toward the understanding and solution of clinical problems.

The electroretinogram is a complicated polyphasic response which varies in its properties with the intensity, size, duration, and wave length of the stimulus and with the state of adaptation of the stimulated retina. When stimuli of short duration are employed, the normal electroretinogram consists mainly of a small, negative deflection (the a-wave) and a larger, positive deflection (the b-wave). These deflections have a definite time relationship to the stimulus. Their shape and amplitude depend upon the factors mentioned above. Two successive electroretinograms taken from an actual record are reproduced in Figure 1.

It is unnecessary to analyze here the normal electroretinogram. Excellent reviews exist which discuss both the physiologic and the clinical aspects of the problem.[1] Suffice it to say that the a-wave is considered to be the expression of an inhibitory process and due largely to cone function, while the b-wave is the electric correlative of the excitatory process taking place in the synaptic layers of the retina, and mainly after stimulation of the rods. The b-wave is believed to be the only electric process transmitted to the optic nerve and has until now been the main criterion for the clinical evaluation of the electroretinogram.

TECHNIQUE

The equipment required for the registration of electroretinograms consists of three main parts: an illuminating device, electrodes for the derivation of the retinal action currents, and a system for the amplification and recording of these currents. The details of the technique employed are of major importance, since they have a decisive influence on the results obtained.

From the Department of Ophthalmology, State University of Iowa College of Medicine.

This work has been supported by a grant from the Arnold Reuben Fight for Sight Fund of the National Council to Combat Blindness.

Read before the Section on Ophthalmology at the One Hundred First Annual Session of the American Medical Association, Chicago, June 11, 1952.

1. (*a*) Granit, R.: Sensory Mechanisms of the Retina, London, Oxford University Press, 1947. (*b*) Karpe, G.: Basis of Clinical Electroretinography, Acta ophth., Supp. 24, 1945. (*c*) Adler, F. H.: Physiology of the Eye: Clinical Application, St. Louis, C. V. Mosby Company, 1950. (*d*) Bounds, G. W., Jr.: The Electroretinogram: A Review of the Literature, A. M. A. Arch. Ophth. **49**:63-89, 1953.

In the standard technique for clinical use developed by Karpe [2] a 25-watt lamp is employed as source of stimulation. At a distance of 140 cm. this lamp gives an illumination of about 20 lux at the eye. A constant rate of stimulation is always maintained (1 flash every 15 seconds);

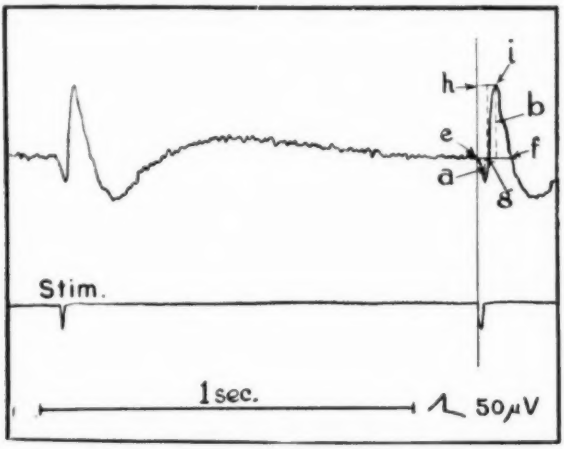

Fig. 1.—Two successive electroretinograms from a normal light-adapted observer. Evaluation of the second electroretinogram is as follows: *a* (height of a-wave), 0.06 mv; *b* (height of b-wave), 0.20 mv; *h-i* (culmination time of b-wave), 53 msec.; *e-g* (latency of b-wave), 25 msec.; *e-f* (duration of b-wave), 88 msec.; *g-f* (duration of b-wave), 63 msec.

Fig. 2.—Stimulating arrangement, with light source in wooden housing.

the duration of the flash is about 1/7 second. In the work reported in this paper an electronically controlled stroboscopic light source ("strobolume," General Radio Corporation) of very

2. Karpe, G.: Apparatus and Method for the Clinical Recording of the Electroretinogram, Docum. ophthalmologica **2**:268-276, 1948.

high intensity was used. With this device the frequency of stimulation could be varied within a wide range (1 to 70 stimuli per second), but the duration of each individual light flash remained always the same (about 3 msec.), regardless of the rate of flicker. The light stimuli employed were thus much more intense and frequent, but also of much shorter duration, than those recommended by Karpe.

The light source was either placed at 50 cm. from the eye to be stimulated or, more frequently, mounted in a cone-shaped wooden housing (Fig. 2). This protected the nonstimulated eye from the light and allowed the insertion of neutral or colored filters at the open end of the box. The stroboscopic light was at 50 cm. from this opening.

The electrodes represent a major technical problem. All types of electrodes recommended by various authors have been tried. Cotton-wick electrodes of the d'Arsonval type, either mounted on a spectacle frame or clamped to a stand and brought in contact with the limbus of the eye, were soon rejected. For trained observers and short experiments these electrodes may be useful, but they are quite inapplicable in clinical routine. The contact with the eyeball is easily lost; the influence of eye movements on the tracings is pronounced, and the need of using a lid retractor necessitates the constant moistening of the cornea. Also, the potentials obtained are considerably smaller than those with a contact-lens type of electrode. Of these electrodes, the one designed by Riggs [3] proved in my hands definitely superior to the Karpe type.[2] The Riggs electrode consists of a plastic contact lens into the contact surface of which on the nasal side a silver disc 2.5 mm. in diameter is inserted flush with the surface (Fig. 3). The silver disc makes

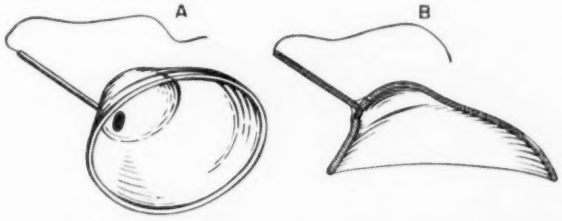

Fig. 3.—Drawing of Riggs contact-lens electrode. *A*, perspective view; *B*, cross section.

contact with a fine wire through a rigid connection. In my experiments this wire was soldered to a regular electroencephalographic lead, through which it connected with the recording device. The contact lens is filled with isotonic saline solution to establish contact with the cornea; the silver disc may be electrolytically coated with silver chloride to avoid polarization, but this precaution does not appear essential.

With the Riggs contact lens, excellent and reproducible electroretinograms can be obtained, and the experiments may be carried on without difficulty for one hour or more. The majority of my recordings so far have been done with this type of electric derivation. However, this electrode, too, has certain drawbacks in the clinical application. If it is used without a speculum (as I have done routinely), blinks may occasionally interfere considerably; the eye tends to slip behind the contact lens, producing movement artifacts; most important, bubble formation may at times make the recording more difficult. This will occur if one does not have a contact lens which fits the patient's eye properly. If one uses individually fitted contact lenses, as does Riggs in his prolonged experimentation with a restricted number of observers, his electrode is doubtless ideal for the purpose. But it is obviously not feasible to use individually fitted contact lenses for clinical routine.

To avoid these difficulties, Mr. Lee Allen has designed, at my suggestion, a new type of electrode which fits all eyes, minimizes the effect of eye movements, and acts as a comfortable speculum (Fig. 4). In addition, it contains leads which permit the derivation of action currents from different parts of the eye. The electrode consists of a corneal contact lens into which a ring

3. Riggs, L. A.: Continuous and Reproducible Records of the Electrical Activity of the Human Eye, Proc. Soc. Exper. Biol. & Med. **48**:204-207, 1941.

of silver wire has been sunken in a groove near the edge of the contact surface. This contact lens is suspended by fine metal springs from a round plastic speculum with handle, such as that used for the gonioprism.[4] In the speculum three silver contact points are embedded, one on each side above and one below. These points make direct contact with the conjunctiva; no fluid is needed. They are connected with each other through the plastic by a fine wire which goes through the handle of the speculum and emerges at its tip. The wire leading from the silver ring in the contact lens leaves it at the lower edge of the circumference. Each of the two wires is soldered to a standard electroencephalographic lead, and electroretinograms can be derived from either lead. The circumference of the speculum contains two openings through which pressure can be applied to the globe with a dynamometer if this is desired. The speculum is easily inserted

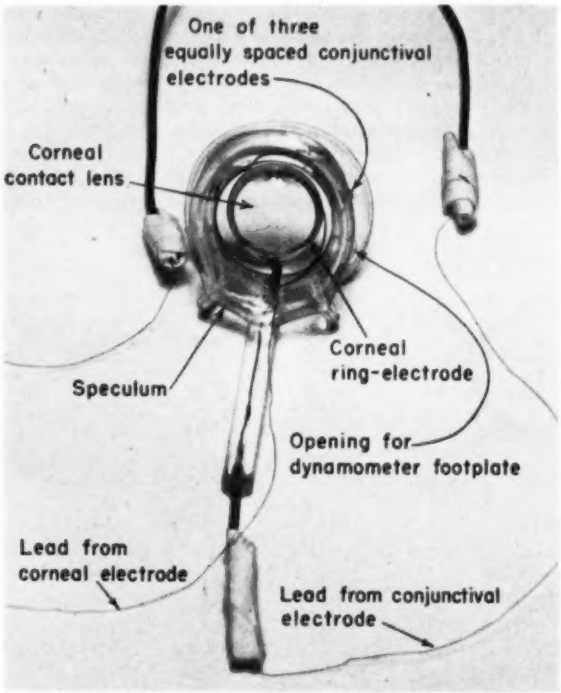

Fig. 4.—Photograph of contact lens-speculum electrode.

between the lids. A small drop of methylcellulose on the contact surface of the lens insures proper adherence to the cornea (Fig. 5). The constructive details of this electrode will be reported elsewhere.

It would, of course, be advantageous if one could dispense altogether with corneal or scleral electrodes, particularly for the recording of electroretinograms in children. An attempt to obtain electroretinograms by placing standard electroencephalographic silver-cup electrodes on the root of the nose and the temple (or the supraorbital or infraorbital region) did not yield usable electroretinograms. Motokawa and Mita [5] used electrodes consisting of tinfoil placed at the root

4. Allen, L., and O'Brien, C. S.: Gonioscopy Simplified by a Contact Prism, Arch. Ophth. **34**:413-414, 1945.

5. Motokawa, K., and Mita, T.: Über eine einfachere Untersuchungsmethode und Eigenschaften der Aktionsströme der Netzhaut des Menschen, Tohoku J. Exper. Med. **42**:114-133, 1942.

of the nose and at the temple and claim to have been able to obtain satisfactory electroretinograms. I have not as yet followed exactly the method suggested by these authors.

To serve as the indifferent electrode, a standard electroencephalographic silver-cup lead was always fastened to the supraorbital (or temporal) area on the side of the eye to be tested. A third electrode was connected to the ear to serve as ground.

Amplification and recording of the retinal action currents were done with a standard four-channel Grass ink-writing electroencephalograph. This yielded excellent tracings and had the advantage that, whenever desired, an electroencephalogram from the occipital cortex could be recorded simultaneously with the electroretinogram. Also, the direct writing simplified the technique, and the amplification was such as to permit an easy evaluation of the recorded tracings. The paper speed used was always 60 mm. per second. In one of the channels the moment of each stimulation was recorded from a photoelectric cell interposed in the path of the stimulus light.

At first the patients were placed in an electrically shielded cage, but this proved to be unnecessary so long as all the equipment in the room was carefully shielded and grounded.

Fig. 5.—Contact lens-speculum electrode in place.

The recordings were made both from light-adapted patients and from relatively dark-adapted patients. The dark adaptation was provided for by completely darkening the room for from 3 to 15 minutes prior to the onset of the stimulation. Between each series of stimulations periods of dark adaptation of 30 to 60 seconds were interposed. When the patient was light-adapted, only brief intermissions were made between the different series of stimulations.

All recordings were made with the patient in a sitting position. The pupils were not dilated routinely; this was done only in exceptional cases. Prior to the insertion of the contact lens, the eye of the patient was anesthetized with 2 drops of tetracaine (pontocaine®) hydrochloride solution, 0.5%. No untoward effect on any eye was noted in the large series of tests.

The evaluation of the tracings consisted of the measurement of the amplitude of the a- and b-waves and of the measurement of the latent period of the b-wave. This was taken to be the time from the moment of the stimulus to the onset of the rise of the tracing above the base line. It was not always easy to determine this point exactly, and I, therefore, also routinely determined the culmination time of the b-wave, defining it for the purpose of this work as the time from the moment of the stimulation to the peak of the b-wave. The total time of the electroretinogram was also measured, this being the time from the moment of stimulation to the moment of return of the b-wave to the base line. If from this value the latent period of

the b-wave is subtracted, the duration of the b-wave can be obtained. All measurements were made with a vernier designed especially by Mr. Lee Allen. The evaluation of the records is indicated in the second electroretinogram of Figure 1.

RESULTS

With this technique, human electroretinograms have been studied for normal and for pathologic eyes over the past two years. In this presentation the results obtained will be reported only in general outline. More detailed discussion is reserved for subsequent papers.

1. *The Normal Electroretinogram.*—The outstanding feature of the human electroretinogram is its b-wave. In conformity with general experience, the ampli-

TABLE 1.—*Decrease in Amplitude of b-Wave with Increasing Stimulus Frequency for a Normal Dark-Adapted Observer*

Stimulus Frequency per Sec.	b Wave, mv.	Amplitude Loss, %
1	0.21	..
2	0.19	10
4	0.15	29
5	0.11	48
7	0.09	57
10	0.06	71
17	0.04	81

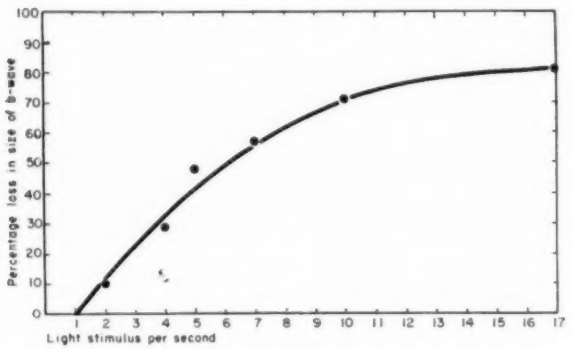

Fig. 6.—Graph showing percentage loss in size of b-potential with increasing stimulus frequency in one experiment.

tude of the b-wave was found to depend to a great extent upon the state of adaptation of the eyes. With more thorough dark adaptation (10 to 15 minutes) the b-wave measured 0.19 to 0.22 mv, decreasing to smaller values when the dark adaptation was less prolonged. With light-adapted eyes the height of the b-wave was usually from 0.12 to 0.15 mv. These figures apply to stimulations with a frequency of 1 per second. With increasing frequency the height of the b-wave decreased with all patients and normal observers. As an example, the figures found in one experiment are presented in Table 1 and Figure 6.

The culmination time of the b-wave and its duration were also affected both by the state of adaptation and by the stimulus frequency. With 1 stimulus per second,

the culmination time in dark-adapted eyes was from 65 to 75 msec., and the total duration was from 110 to 125 msec. With 2 stimuli per second, it was usually slightly larger, and it then decreased with increasing stimulus frequency, reaching about one-half to two-thirds the initial value with 17 stimuli per second. For light-adapted eyes the initial values were about 45 to 50 msec. for the culmination time and 65 to 85 msec. for the total time, with a proportionate decrement as the stimulus increased in frequency. The latent period of the b-wave was, however, little influenced either by the state of dark adaptation or by the stimulus frequency; it was usually approximately 20 to 25 msec.

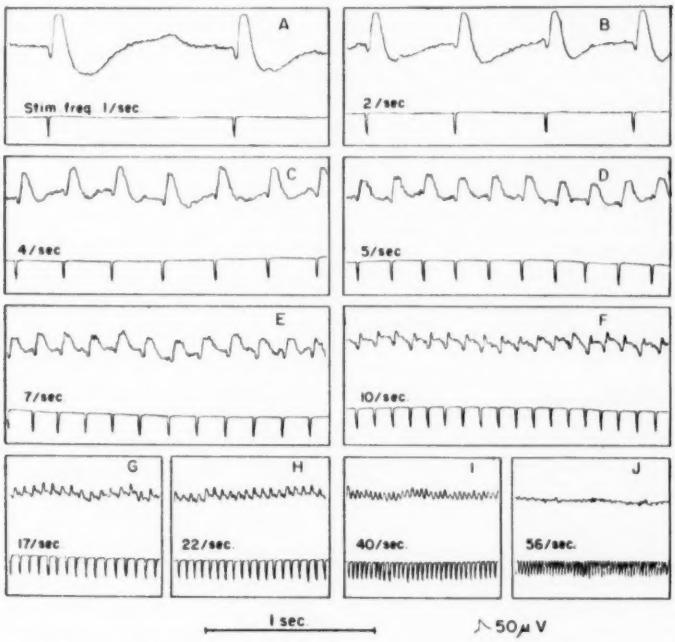

Fig. 7.—Series of electroretinograms at 10 selected stimulus frequencies, showing decrease in b-wave, appearance of sinusoidal rhythm (*I*) and extinction of electroretinogram (*J*).

In all records a measurable a-wave was noted, but it tended to be less stable than the b-wave. For the lower stimulus frequencies (6 to 7 stimuli per second) it was regularly greater in the light-adapted eye. In both the light- and the dark-adapted eyes there was some decrease in the height of the a-wave with increased stimulus frequency, but this decrease was less regular than for the b-wave and was generally only 20 to 30% of the initial value when the stimulus frequency reached 17 stimuli per second. The initial values (1 stimulus per second) were generally about 0.04 to 0.05 mv for the light-adapted eye and 0.03 to 0.04 mv for the dark-adapted eye.

Thus, the size of the a- and b-waves tended to approach each other with higher stimulus frequencies, and there was a point at which the response of the retina assumed more and more the shape of a sinusoidal wave, which finally flattened out

to become more or less a straight line at very high frequencies. A sample series of electroretinograms at 10 selected frequencies, showing the decrement of the a- and b-waves and the final absence of response, is reproduced in Figure 7.

It was, of course, of interest to correlate the changes in appearance of the electroretinogram with the subjective critical flicker fusion frequency. The stroboscopic light in the arrangement used in this study was not an ideal method for determining the critical flicker fusion frequency. At the edges of the stimulating light a flicker could be noted even with the highest frequencies employed, but if the observer was requested to concentrate his attention on the central part of the lamp, good agreement was obtained from all observers. With a stimulus frequency of 17 per second all observers noted a definite flicker; with 22 stimuli per second most observers were not sure whether a flicker was present, but with 25 to 28 stimuli per second the central flicker had definitely disappeared. In other words, when the retinal response had assumed a sinusoidal form, the individual stimuli were fused.

2. *Effect of Compression of Globe on the Electroretinogram.*—Because of the great sensitivity of the retina to anoxia and the well-known "black-out" which occurs when pressure is applied to the eyeball, it was thought to be of interest to determine the behavior of the electroretinogram during compression of the globe.

In the preliminary experiments, reported here, the patient himself exerted finger pressure upon the globe from the temporal side, keeping the pressure as even as possible. The result was an almost immediate decrease of the b-wave, with a slight rebound after about 10 seconds. Within 25 to 30 seconds the size of the b-wave was reduced to approximately 35% of the initial value, and at this point the observers would report that they were "blind." In spite of this, however, a measurable b-wave continued to be recorded for another 20 to 30 seconds. The a-wave also underwent a certain reduction in size, and there was a considerable increase in the culmination time and the total time. In 30 seconds the culmination time in one observer increased from 45 to 61 msec., and in another, from 86 to 108 msec.; the corresponding total times increased from 107 to 136 msec. and from 146 to 185 msec., respectively.

When the pressure was released after a compression lasting 90 to 110 seconds, the first electroretinograms appeared immediately. They were again characterized by longer duration and by small b-waves, but the most striking feature was the appearance of a very pronounced a-wave, which in one observer, for instance, reached 66-71 mv. as opposed to 16 mv. prior to compression. Vision was regained after 15 to 20 seconds, but the electroretinograms were not fully normalized for two or three minutes, or even more.

The compression test was also performed on a patient with absolute glaucoma in one eye and no sign of glaucoma in the other eye. The normal eye behaved much like the normal controls; the glaucomatous eye showed no rebound and a much faster loss in the amplitude of the b-wave than the normal, fellow eye. The findings concerning the b-wave in this patient and in a normal control are summarized in Table 2; the percentage losses in height of the b-wave are reproduced in a graph (Fig. 8). These compression experiments are now being put on a quantitative basis with regard to amount and duration of pressure by my collaborator, Dr. George W. Bounds Jr., in an attempt to develop a functional test for early glaucoma and other ocular disorders.

3. *Simultaneous Registration of the Electroretinogram and the Electroencephalogram.*—The simultaneous registration of the electroretinogram and the electro-

encephalogram from the occipital region is of particular interest. It has been pointed out by Monnier and his co-workers [6] that the determination of the temporal relationship of the retinal and cortical responses acquires importance in cases of lesions of the optic pathways. It is all the more interesting to study the two conjointly in the presence of a functional loss of visual acuity, such as exists in amblyopia ex anopsia. In this section attention will be called only to this condition.

To obtain an insight into the functioning of the optic pathways, one can measure the time which elapses between the retinal response and some cortical reaction produced by the light stimulus. This cortical reaction may be either the blocking of

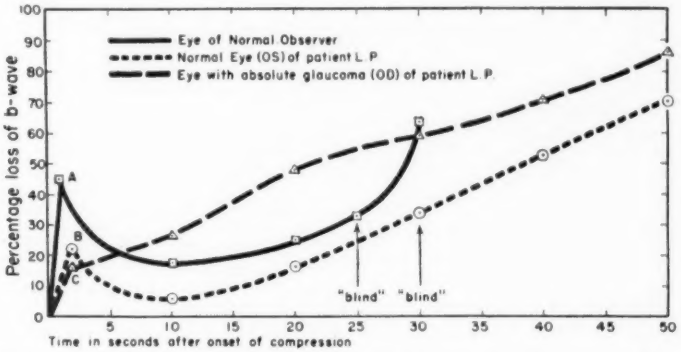

Fig. 8.—Graph showing percentage loss in size of b-potential during compression of globe in two normal and in one glaucomatous eye.

TABLE 2.—*Loss of b-Wave During Compression of Globe**

Time, in Sec., After Start of Compression	Normal Control	Patient L. P.	
		Normal Eye (O. D.)	Glaucomatous Eye (O. S.)
1	0.12	....	....
2	....	0.14	0.12
10	0.16	0.17	0.11
20	0.14	0.15	0.08
25	0.12 ("blind")	....	....
30	0.06	0.12 ("blind")	0.06
40	....	0.088	0.043
55	....	0.056	0.038
60	....	0.019	0.020
Prior to compression (average of 30 successive ERG's)	0.19 ± 0.014	0.18 ± 0.015	0.15 ± 0.016

* The patients were dark-adapted. The stimulus frequency was 2 per second. The height of the b-wave is expressed in millivolts.

6. (*a*) Monnier, M., and Jeanneret, R.: Contrôle objectif de la conductibilité des voies-optiques centrales par l'électro-rétinographie et l'électro-encéphalographie combinées, Ophthalmologica **113**:1-11, 1947. (*b*) Monnier, M., and Boehm, F.: Prufung der Leistungsfähigkeit des optischen Systems durch kombinierte Elektroretinographie und Elektroencephalographie beim Menschen, Helvet. physiol. et pharmacol. acta **5**:C34-35, 1947. (*c*) Monnier, M.: Mesure du temps rétino-cortical à partir des potentiels corticaux évoqués par stimulation lumineuse chez l'homme, ibid. **6**:61-62, 1948.

the alpha rhythm or the appearance of cortical rhythms evoked by the light stimulus (photic driving). I have chosen the latter criterion because it is more easily measured, and have determined the cortical culmination time (CT_c), that is, the time elapsed from the moment the stimulus was applied to the moment of the peak of

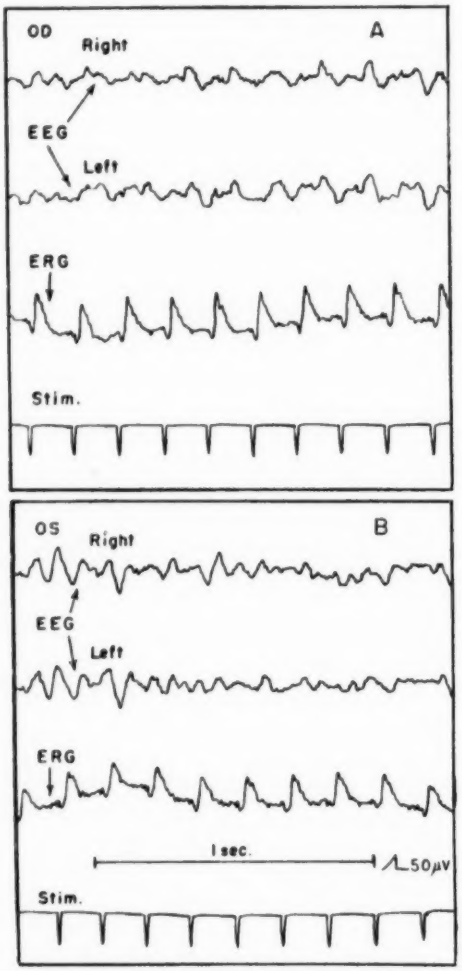

Fig. 9.—Simultaneous recording of electroretinogram and electroencephalogram of patient with amblyopia ex anopsia. *A*, normal (right) eye (visual acuity 20/15) exposed to light stimulation: definite photic driving. *B*, exposure of amblyopic (left) eye (vision equal to counting fingers at 1 meter) to light stimulation: doubtful photic driving; alpha rhythm persisting.

the cortical response. When from this the culmination time of the b-wave (CT_b) is deducted, a measure for the central transmission time (CTT) is arrived at. In a series of normal subjects, and with a stimulus frequency of 4 per second, a central transmission time (CTT) of 115 ± 15 msec. was arrived at.

The responses obtained in eyes with amblyopia ex anopsia vary with different patients. If the visual acuity is rather low, one may find, as has been reported elsewhere,[7] that the occipital cortex may respond with rhythmic discharges to rhythmic light stimulation of the normal eye, while it may fail to do so when the amblyopic eye is stimulated. In fact, in such a case an alpha rhythm may be present in spite of the fact that the eyes are open and the amblyopic eye is stimulated by light. Normally the alpha rhythm is absent under these conditions. An example of this type of behavior is reproduced in Figure 9.

In other patients, especially if the visual acuity is not too low, photic driving may be elicited from the amblyopic eye, but its amplitude may not be as great as when

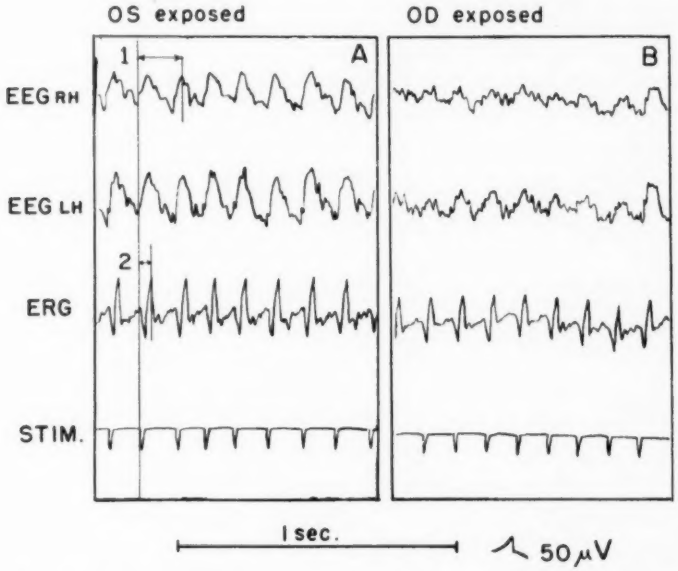

Fig. 10.—Simultaneous recording of electroencephalogram and electroretinogram. EEG_{RH} is tracing from right occipital cortex; EEG_{LH}, tracing from left occipital cortex. *A*, shows tracing for normal (left) eye (visual acuity 20/15) exposed to light. *1* indicates cortical culmination time (CT_c); *2*, culmination time of b-wave (CT_b); *1-2*, central transmission time (CTT). The tracing shows excellent driving from both eyes but pronounced difference in amplitude.

the normal eye is driven; the driving may be more irregular, and there may be differences in the response from the two hemispheres. Also, the central transmission time may be prolonged in comparison with that on stimulation of the normal eye. Such a case is illustrated in Figure 10.

4. *The Electroretinogram in Diseases of the Eyes.*—With the technique described, electroretinograms were recorded from patients with cataract, glaucoma, optic nerve atrophy, retinal detachments, and retinitis pigmentosa.

7. Burian, H. M., and Watson, C. W.: Cerebral Electric Response to Intermittent Photic Stimulation in Amblyopia ex Anopsia, A. M. A. Arch. Ophth. **48**:137-143, 1952.

The findings were in good agreement with those reported by previous investigators. Electric responses were obtained from all eyes with peripheral retinas capable of functioning, regardless of visual acuity or extent of visual field. Clouding of the media affected the electroretinogram only so far as it reduced the amount of light reaching the retina. With clear media normal electroretinograms were obtained even from blind eyes, provided the blindness was not due to a retinal affection. Thus, in many eyes with optic nerve atrophy the electroretinogram may remain normal over a long period.

The same was found to be true for patients with absolute glaucoma. In a patient who had absolute glaucoma in the right eye and who had had no vision in that eye for over one year the b-wave measured 0.15 mv. (eye dark-adapted; stimulus frequency, 2 per second). The normal, fellow eye, under the same experimental

TABLE 3.—*Effect of Reduction of Light Intensity by Means of Neutral Filter on Size of b-Wave in Normal and Glaucomatous Eye of a Patient*

Stimulus Frequency per Sec.	b-Wave, in mv	
	Normal Eye (O. S.)	Glaucomatous Eye (O. D.)
1	0.17	0.12
2	0.16	0.11
4	0.13	0.08
6	0.08	0.04

TABLE 4.—*Size of a- and b-Waves, in Millivolts, of Patient D. C.**

Stimulus Frequency per Sec.	O. D.		O. S.	
	a-Wave	b-Wave	a-Wave	b-Wave
1	0.071	0.18	0.043	0.042
2	0.074	0.16	0.039	0.041
3	0.059	0.15	0.033	0.035
4	0.066	0.14	0.026	0.031

* The right eye was normal; the left eye was operated on for traumatic detachment. The eyes were dark-adapted.

conditions, had a b-wave of 0.17 mv. It was noted that the pupil of that eye was relatively narrow, while that of the glaucomatous eye was wide (7 mm. in diameter) and fixed. After dilation of the pupil of the normal (left) eye to a width of 7 mm. to equalize the pupillary diameters of the two eyes, the b-wave had a height of 0.19 mv. In another experiment on this patient a neutral filter was interposed in the path of the stimulating light to reduce the light intensity. The effect of this on the size of the b-wave was much more pronounced in the glaucomatous eye than in the normal eye (Table 3).

In the patients with retinal detachment the electroretinograms were either extinguished or subnormal. In one patient, with an extensive traumatic retinal detachment of the left eye and a visual acuity limited to light perception in that eye, the electroretinogram was found to be extinguished when recording was done seven weeks after the injury. One month after operation the patient's retina was observed to be reattached except for the extreme periphery below, but his vision

was only 4/60, owing to a large hole in the macula. The electroretinogram taken at that time was subnormal, with a b-wave of 0.04 to 0.03 mv. The corresponding a-wave was relatively very large, being of about the same size as the b-wave (Table 4).

In patients with retinitis pigmentosa the electroretinogram was found to be extinguished.

COMMENT

The properties of the normal electroretinogram obtained with the method described in this paper differ in certain respects from those of the electroretinogram which the standard method of Karpe has yielded. This is not surprising when one considers that the light stimulus employed was considerably stronger and of shorter duration that that with Karpe's method, and that the lowest stimulus frequency used was 1 light flash per second. In my electroretinograms the b-wave was of smaller amplitude, but it was also of shorter duration and had a shorter latent period.

One would expect that the values reported by Euzière, Passouant, and Cazaban in a recent paper [8] would more nearly agree with those found by me, since these workers stimulated the retina with electronically controlled light flashes, similar to those I employed. However, the b-waves in the electroretinograms of these authors varied from 0.09 to 0.15 mv. with an average of 0.11 mv. The amplitude was thus lower than that I recorded. Also, the duration of the b-wave was greater (148 msec.) and the latent period longer (47 msec.). It is probable that the differences between the figures found by the French authors and those found by me are accounted for by the fact that the former used a cotton-wick electrode placed in the lower cul-de-sac and my electroretinograms were obtained with contact-lens electrodes.

Nevertheless, there appears to be conformity in the general configuration of the electroretinograms in my tracings and the tracings of Euzière and his collaborators. But two noteworthy discrepancies in our findings must be pointed out. One is that Euzière, Passouant, and Cazaban state that the b-wave of the electroretinogram remains normal with stimulus frequencies of up to 4 light flashes per second and that the b-wave disappears with 5 flashes per second. I have found, on the contrary, that the amplitude of the b-wave decreases immediately with each increase in stimulus frequency and that, while its size is reduced about one-half with 5 to 7 light stimuli per second, it is still about one-fifth the original height with 17 flashes per second (Fig. 6). One cannot speak of a disappearance of the b-wave until much higher frequencies are reached (Fig. 7).

The second discrepancy in our findings relates to the subjective flicker fusion frequency. Whereas my observers unanimously reported fusion of the light stimulus with frequencies of 22 to 25 flashes per second, which is in accordance with observations of Babel and Monnier,[9] Euzière and his collaborators found a flicker fusion frequency of 52.

In one important point there is, however, agreement in the results of Euzière, Passouant, and Cazaban and mine, and that is the presence in all our electroretino-

8. Euzière, J.; Passouant, P., and Cazaban, R.: Temps objectifs de fusion et excitations lumineuses doublées en électro-rétinographie, Ann. ocul. **184**:865-876, 1951.

9. Babel, M., and Monnier, M.: Détermination objective de la fréquence de fusion par l'électro-rétinographie chez l'homme, Helvet physiol. et pharmacol. acta **7**:4-5, 1949.

grams of an a-wave of significant amount. Karpe has purposely attempted to simplify the electroretinogram for clinical purposes, and he and his school have concentrated their attention mainly on the b-wave. It appears that this deprives us of an interesting tool in the study of the electroretinogram, and I quite agree with Wirth [10] that the study of the various components of the electroretinogram should be extended to man, especially clinically. But I cannot ascribe to his opinion that the appearance of an a-wave in man is a pathologic phenomenon.

Physiologic and clinical evidence indicates that the electroretinogram, and specifically the b-wave, is mainly the result of stimulation of the rods; it is a scotopic retinal response. The a-wave, on the contrary, seems to be largely a photopic reaction, closely connected with the cone function. Thus far the electroretinogram has been almost exclusively a means of investigating the function of the retinal periphery. It has told nothing of the intactness or the functional quality of the macula. Investigations are now being carried out with the aim of creating stimulus situations better adapted to the production and study of a-waves and macular responses.

The importance of having at one's disposal appropriate methods for the appraisal of the a-wave is emphasized by two observations, which may have the same, or a related, explanation. In the compression experiments reported above, it was noted that on release of the pressure abnormally large a-waves occurred, and it was further noted in a patient with retinal detachment (Table 4) that upon partial return of function of the retina the a-wave was very large relative to the b-wave. In partially functioning retinas the a-wave appears to have a proportionately greater significance than in the normally functioning retina. This observation agrees with the findings of Karpe,[1b] who found a large a-wave and a diminished b-wave in a patient with an embolus in a small branch of the central retinal artery and a "negative" electroretinogram in a number of other conditions.

During the compression experiments just alluded to the observers reported that their vision blacked out when the b-wave had been reduced to about one-third its initial value. In spite of the fact that the observers were subjectively blind, a b-wave continued to be recorded for a considerable time if the pressure on the globe was kept up. It has been shown, on the other hand, that there is no change in the subjective brightness of the stimulus light, even if the size of the b-wave is reduced to zero by increasing the stimulus frequency. Different mechanisms enter into play in these two situations. The size of the b-wave is in itself not a sufficient index for the subjective visual reaction; that reaction depends on the intactness of the whole visual pathway.

The question arises: To what is due the decrement of the b-wave which arises with increasing stimulus frequency? The size of the b-wave is determined to a great extent by the state of adaptation of the eye. One must assume that with each increase in the rate of flicker the eye becomes more light-adapted, since the interval between stimulations is shortened. But within each series of stimulations with one frequency—even with the high ones—there is no evidence from the size of the b-wave that the eye becomes progressively light-adapted. There is no systematic

10. Wirth, A.: (*a*) Caratteri dell'elettroretinogramma nell'uomo, Ann. ottal. e clin. ocul. **76**:109-123, 1951; (*b*) Beiträge zu den Teilströmen des menschlichen Elektroretinogramms, von Graefes Arch. Ophth. **151**:662-671, 1951.

decrease in the amplitude of the b-wave, even if the stimulation is continued for many seconds. Except for the very first response, which has always a much larger b-wave, the size of all b-waves within one series remains the same. It appears that for each frequency an equilibrium is established. The size of the b-wave depends on the time interval elapsed since the preceding stimulus reached the retina. If the time interval is kept constant, the b-wave also remains constant. The larger the time interval, the larger the b-wave; the shorter the time interval, the shorter the b-wave. Thus, it is not the state of adaptation per se which determines the relative size of the b-wave in these flicker experiments, but, rather, the fact that for a given flicker frequency the process of restitution within the retina is interrupted at the same point with each succeeding stimulation.

The sensation of brightness is not affected by changes in the stimulus frequency. The stimulus propagation remains normal, regardless of the size of the b-wave. Not so in the compression experiment. Here the visual sensations are lost in spite of the presence of large b-waves, indicating that the initial impairment caused by the anoxia or the actual mechanical compression occurs within the neural pathways. Noell [11] has reached the same conclusion and believes that it is most likely that the block is initially established within the ganglionic cell neuron.

Similar considerations apply to the eyes of patients with advanced glaucoma who have little or no vision and a very deficient visual field. Such eyes may show a normal b-wave under ordinary test conditions, indicating that the process of retinal excitation is not primarily involved. The block of the impulse propagation must be located in the neural pathways. But if functional tests are performed on such eyes, if pressure is applied to the globe (Table 2), or if the light intensity is reduced (Table 3), the depression of the b-wave is far more pronounced than in normal eyes. This is evidence that the process of retinal excitation is secondarily damaged.

Electroretinography may thus contribute to the understanding of disease processes in the eyes, but it is not primarily a diagnostic tool. At present its chief clinical value lies in the fact that it may be helpful in establishing the prognosis in certain cases. But it will not achieve its full clinical significance until functional electroretinographic tests have been developed. An important step in this direction is the work of Henkes,[12] who has studied the effect of vasodilating drugs on the electroretinogram and believes that it offers a means of deciding which vasodilator is most appropriate by determining objectively the amount and duration of the effect of the drugs under consideration. The development of a compression test, the development of a test for macular function, the use of graded neutral filters, etc., should further enhance the clinical value of electroretinography.

It should become of special importance in a field which lies beyond the reach of the ophthalmoscope, i. e., the evaluation of the function of the optic pathway. As has been pointed out, both in organic and in functional lesions of these pathways the determination of the central transmission time may acquire considerable interest, provided that proper standards can be established. In my records the

11. Noell, W. K.: Site of Asphyxial Block in Mammalian Retinae, J. Appl. Physiol. **3**:489-500, 1951.

12. Henkes, H. E.: Use of Electroretinography in Measuring the Effect of Vasodilation, Angiology **2**:125-131, 1951.

normal central transmission time, as determined by the appearance of evoked cortical responses, was about 115 ± 15 msec. Monnier, using the same criterion, found about 50 ± 15 msec.[6c] The difference in our figures is largely to be attributed to a difference in the latent period of the b-wave. When the alpha blocking time was used as criterion of cortical response, the central transmission time was found to be much longer, but also less stable, measuring 185 ± 60 msec. (Monnier and Boehm[6b]).

SUMMARY

The technique used in this study of the human electroretinogram consisted of light stimulation with electronically controlled stroboscopic light flashes of high intensity and variable frequency, derivation of the retinal action currents with contact-lens electrodes, and amplification and recording with a direct ink-writing encephalograph.

The properties of the normal electroretinograms obtained with this method are described and evaluated.

The influence of compression of the eyeball on normal and on glaucomatous eyes is discussed.

Attention is drawn to the combination of electroretinography with electroencephalography for the study of functional disturbances, such as amblyopia ex anopsia.

The future progress of clinical electroretinography is expected to come from the development of functional tests for early detection of certain ocular diseases, from the development of tests for macular function, and from the combined investigation of the electroretinogram and the electroencephalogram in the appraisal of the function of the optic pathways.

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ROENTGEN-RAY CATARACT

Effects of Shielding of the Lens and Ciliary Body

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THE OCCURRENCE of cataract following exposure of the lens to ionizing radiations has been demonstrated on numerous occasions, both in man and in experimental animals. Cataract occurs in varying degree, depending upon the quality of the radiation, the total number of roentgens given, and the interval of time during which the exposure is made. Thus, a specific amount of the longer roentgen rays given in a single dose is more cataractogenic than the same r dosage of short rays given in divided doses over a period of several days or weeks. In addition, the cataractous reaction in the lens, which becomes visible only after a variable latent period, depends upon the species and the age of the animal exposed to radiation. These circumstances have resulted in considerable confusion concerning not only the ultimate occurrence of cataract and the relationship to radiation, but likewise the fundamental cause of the lens opacification. Most observers consider the injury to occur primarily in the lens, as a result of direct damage either to the epithelium or to the lens fibers and their proteins. The nature of this change has been considered by most observers to be an alteration in the chemical, enzymatic, physical, or cellular processes of the lens which occurs as a direct result of the radiation. Others believe that the lens damage is indirect, caused by the impaired nutrition that results from injury to the blood vessels of the ciliary body. In order to test the validity of these hypotheses, we devised the experiments to be recorded so that either the ciliary body or the lens could be selectively submitted to a cataractogenic dose of roentgen rays. Protection of the desired tissues was secured by making appropriate shields from sheet lead 2 mm. in thickness.

EXPERIMENTAL PROCEDURE AND RESULTS

Five lead shields 2 mm. in thickness were employed in the course of these experiments (Fig. 1), each one designed primarily to protect certain portions of the lens or the eye from direct irradiation, and, in addition, to exclude, so far as possible, other structures. In each experiment one of these shields was sewed with 4-0 black silk to the sclera of one eye of young albino rabbits of approximately 2-kg. weight, while the animal was under pentobarbital anesthesia. The holes

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through which the silk thread passed were drilled obliquely. The shielded eye was then exposed in a direction perpendicular to the cornea to a coned beam of an x-ray machine. The following factors were employed in all cases: 120 Kv.; distance from the x-ray source to the exposed eye 26 cm.; half-value layer, 3 mm. Al. One thousand roentgens in air, an amount estimated to be cataractogenic, was the routine experimental dose. In a few instances, as indicated, a larger dose was arbitrarily given. All experiments are summarized in the accompanying Table.

Six rabbits comprised the first group, 1A, to each of which a round lead shield 13 mm. in diameter [1] (Fig. 1*a*) was sewed in place overlying the cornea of the right eye. This protected the lens from the radiations directed toward it. For five animals the dose was 1,000 r, while for one it was arbitrarily increased to 1,500 r. Lens opacities did not develop in any of the directly irradiated eyes, but in three of the five fellow eyes opacities developed, since they were not adequately shielded from the direct x-ray beam.

In Group 1B, a 4-cm. circular lead shield with a central opening 13 mm. in diameter (Fig. 1*b*) was sewed to the right eye of each of six rabbits. This per-

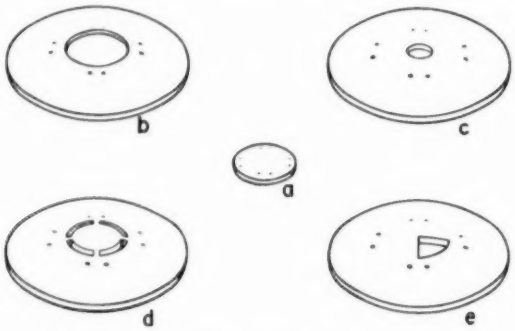

Fig. 1.—Lead shields used in the experiments.

mitted exposure of the lens to 1,000 r in five rabbits and to 1,500 r in one, while the ciliary body and other occular tissues were protected. In all five of the directly irradiated eyes in Group 1B opacities developed (Fig. 2, left) in the lens. The heavier exposure resulted in the same type of opacities, but they occurred earlier than those following the smaller dose. All the fellow eyes retained clear lenses, for the shield was wide enough to cut off the peripheral rays of the beam, which would otherwise have reached the fellow eye.

Group 1C consisted of two rabbits which were given 1,000 r in air, with the same factors as above, and with the rays directed to one eye according to routine, except that no shield was employed. In all four eyes characteristic opacities (Fig. 2, left) developed.

In Group 2A, a lead shield 4 cm. in diameter with a 5-mm. central aperture (Fig. 1*c*) was sewed to the right eye of each of seven rabbits. In four animals a dose of 1,000 r in air and in the remaining three animals a dose of 2,000 r were directed to the shielded eye of each animal. Cataract did not develop in any of the

1. This size was determined after in situ measurement of a number of lenses of control eyes.

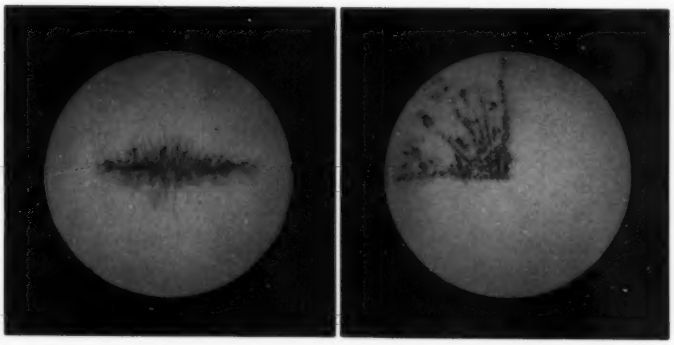

Fig. 2.—Left, typical posterior subcapsular opacities produced by irradiation of the entire lens; right, posterior subcapsular opacities produced by irradiation of one quadrant of the lens.

treated eyes, but in six of the fellow eyes typical opacities occurred. Figure 1 *c* illustrates the shield used in Group 2A.

Group 2B represents an attempt to direct the radiation to the periphery of the lens of one eye of each of three rabbits. An opening 1 mm. wide was made in a lead shield (Fig. 1 *d*), exposing the area 5.5 to 6.5 mm. from the center to the standard experimental radiation of 1,000 r in air. The area of the opening in this shield was computed to be the same as the 5-mm. aperture of Figure 1 *c*. The shield is illustrated in Figure 1 *d*. Cataract developed in the lens of both eyes of these animals.

Results of Exposure of Rabbit Eyes to Roentgen Radiation, Using Five Types of Eye Shields

Rabbit	Irradiated Eye *	Fellow Eye *	Shield	Dose Comment
1A 1	—	+	a	1,000 r
1A 3	—	+	a	1,000 r
1A 5	—	+	a	1,000 r
1A 7	—	+	a	1,000 r
1A 9	—	+	a	1,000 r
1A 11	—	+	a	1,500 r
1B 2	+	—	b	1,000 r
1B 4	+	—	b	1,000 r
1B 6	+	—	b	1,000 r
1B 8	+	—	b	1,000 r
1B 10	+	—	b	1,000 r
1B 12	+	—	b	1,500 r
1C 13	+	+	None	1,000 r
1C 14	+	+	None	1,000 r
2A 1	—	—	c	1,000 r
2A 3	—	+	c	1,000 r
2A 5	—	—	c	1,000 r Died 121st day
2A 7	—	+	c	1,000 r Died 161st day
2A 9	—	+	c	2,000 r
2A 10	—	+	c	2,000 r
2A 12	—	+	c	2,000 r
2B 2	+	+	d	1,000 r
2B 4	+	+	d	1,000 r
2B 6	+	+	d	1,000 r
2C 14	+	+	e	Opacities limited to irradiated quadrant
2C 15	+	+	e	Opacities limited to irradiated quadrant

* The plus sign (+) indicates cataract formation; the minus sign (—), no cataract formation.

In a final group, of two rabbits, 2C, the right eye was given 1,000 r. The shield in this experiment (Fig. 1 *e*) was made in such a manner that all the lens except the upper temporal quadrant was protected. The pie-shaped sector opening in the shield extended over one quadrant and had a radius of 6.5 mm. Typical posterior subcapsular opacities, which were sharply limited to the quadrant exposed (Fig. 2, right), developed in both animals.

COMMENT

These experiments again demonstrate the relation of roentgen radiation to cataract and, in addition, indicate the direct association of exposure of the lens to the development of lens opacities. When, as shown, the lens is protected from

radiation, no cataract occurs, even though the ciliary body receives the dose that would be sufficient to produce cataractous changes. Furthermore, the experiments in which the equatorial region of the lens is subjected to irradiation disclose that the more actively growing portion of the lens, the lens epithelium and fibers of the equatorial region, are especially sensitive, and exposure of this region yields the same results as irradiation of the entire lens. As a corollary of this, the experiments show that the more central segment of the lens (the 5-mm. pupillary zone) is relatively insensitive, and twice the dose that produces cataract on exposure of the peripheral portion is ineffective centrally. This is to be expected, since the more actively dividing epithelial cells at and near the equator should be most sensitive to injury by the radiation. Evidence of injury to the cells of the more central portion of the lens epithelium, because of the slow growth of these cells, as indicated by their low mitotic index, would be minimal in amount. The very slow growth or the x-ray-induced absence of mitosis of these epithelial cells could so delay their eventual migration to the equatorial region that objective evidence of injury might never be observed. Some of these injured cells may undergo pyknosis and disappear completely.

The experiments in which the exposure of the lens was limited to one quadrant substantiate the view that cataract is the result of a local effect of the irradiation. In these experiments the changes observed in the one quadrant were those that would be obtained in that quadrant if the entire lens had been exposed, but, because of protection, the three unexposed quadrants remained clear. There was definitely no general or diffuse effect. One is therefore permitted to conclude that roentgen radiation induced some type of change in the lens which is limited to the region of exposure, and which seems to be due to injury of the more equatorial portion of the lens. The cataractous change so induced appears after a latent period, which, together with the histologic changes previously observed, indicates injury to the lens epithelium.

The dose of roentgen rays used in these experiments was not sufficient to produce complete cataract. In interpreting these partial opacities in the lens, we have not considered the changes that might be caused by much larger doses, amounts which might induce changes in capsular permeability or actual denaturation of lens protein.

In most instances the shields did not protect the opposite eye, and cataract occurred because of direct injury by the radiation. The occurrence of cataract in the opposite eye thus acted as a positive control of the cataractogenic character of the radiation used.

CONCLUSIONS

1. Exposure to roentgen rays does not cause cataract when the lens is protected by a lead shield 2 mm. thick.

2. The actively growing equatorial portion of the lens appears to be most sensitive to injury by roentgen rays.

3. The pupillary zone of the lens appears to be the least sensitive.

4. Exposure of one quadrant of the lens to roentgen rays results in opacities limited to that quadrant.

Drs. H. D. Kerr and H. B. Elkins, of the Department of Radiology, and Dr. T. C. Evans, of the Radiation Laboratory, gave assistance and use of the facilities of their laboratories in this study. Mr. Robert Herring assisted in the experiments and in the care of the animals.

MENINGIOMAS OF ANTERIOR CLINOID PROCESS AS A CAUSE OF UNILATERAL LOSS OF VISION

Surgical Considerations

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MENINGIOMAS constitute approximately 15% of all intracranial tumors. They appear to arise from clusters of arachnoid cells and tend to occur in specific sites.

Meningiomas, because of their pathologic appearance and their lack of invasive properties, are considered benign tumors. However, their slow and frequently silent growth permits them to attain considerable size before surgical intervention is required because of obvious neurologic disturbance. To prevent a recurrence of the tumor, its complete extirpation is desirable. The size of the tumor frequently precludes its complete removal. The mass frequently becomes attached to important blood vessels and parasellar structures, making its removal hazardous (Fig. 1). The relatively high incidence of postoperative complications and the relatively high mortality rate associated with the removal of meningiomas situated in certain portions of the brain offer a challenge to the clinician and the neurologic surgeon.

If the tumor is situated at certain places within the cranial vault, few symptoms may appear to indicate a growing intracranial tumor until the mass has attained considerable size. This fact is well recognized and offers a diagnostic challenge. We have become especially interested in meningiomas of the anterior clinoid processes of the sphenoid bone because the loss of vision produced by the direct pressure of the tumor on one optic nerve may be the only symptom of the lesion for many years.

In most cases loss of vision is the symptom which causes the patients to seek early medical attention. The future course is largely in the hands of the physician, who must determine the cause of the loss of vision and prescribe early treatment, if any, to remove this cause. Although we wish to stress the importance of recognizing unilateral blindness, which may result from a meningioma, it is hoped that the diagnosis of the cause can be made before complete loss of vision occurs.

We recently have had the opportunity to study several cases in which unilateral loss of vision developed over a period of many years. Several different diagnoses

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had been made in these cases, and the patients had lesions which were amenable to early surgical treatment. We also have reviewed the records of 310 cases in which patients came to the Mayo Clinic chiefly because of unilateral loss of vision in the years 1940 to 1944 inclusive. The lesions responsible for the loss of vision in these cases are listed in Table 1. It is interesting that in 108 (34.8%) of the 310 cases lesions involved the retrobulbar portion of the optic nerve. It is this portion of the optic nerve that is injured by a meningioma of the anterior clinoid process. A meningioma was found to be responsible for unilateral blindness in 15 of the 108

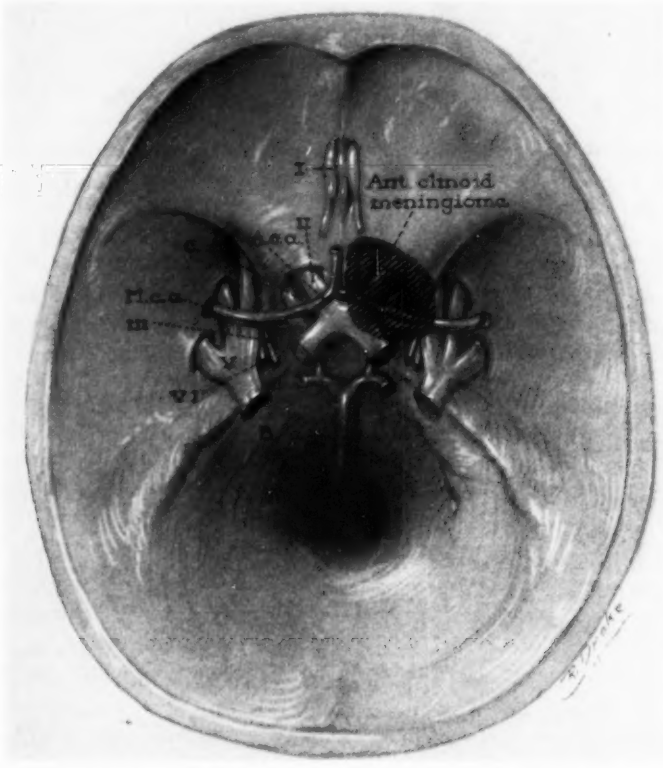

Fig. 1.—Diagrammatic sketch of right anterior clinoid meningioma superimposed over structures in base of skull: *I*, olfactory nerve; *II*, optic nerve, left; *III*, third cranial nerve; *V*, fifth cranial nerve; *VI*, sixth cranial nerve; *A.c.a.*, anterior cerebral artery; *C.s.*, carotid siphon; *M.c.a.*, middle cerebral artery; *B.a.*, basilar artery.

cases in which the unilateral blindness was due to a variety of lesions of the optic nerve and visual pathways (Table 2).

From these and other findings, it is apparent that the possibility of a surgical lesion being responsible for unilateral loss of vision must always be considered. Therefore, a complete examination, including roentgenographic studies of the skull, ophthalmoscopic examination, and determination of the visual field, is of extreme importance, so that early recognition of the cause of loss of vision can be made and

early treatment instituted. If the possibility of a lesion amenable to operation is considered in all cases of visual defects, the patients can receive definitive treatment before they have lost the vision in one eye.

During the 21-year period from 1930 to 1950 inclusive, 52 patients who had meningiomas arising from the region of the anterior clinoid process were treated surgically, with a postoperative mortality of 32.7%.

It is apparent that early diagnosis is essential if surgical removal of these tumors is to be successful, because a tumor which grows to surround intimately the anterior portion of the circle of Willis and to involve the third ventricle and hypotha-

TABLE 1.—*Causes of Unilateral Loss of Vision in 310 Cases*

Cause	Cases	
	No.	Per Cent
Lesions of structures of eyeball	82	26.5
Glaucoma	72	23.2
Trauma	40	12.9
Congenital lesions	7	2.3
Functional conditions	1	0.3
Lesions of the optic nerve or visual pathways	108	34.8
Total	310	100.0

TABLE 2.—*Lesions of the Optic Nerve or Visual Pathways in 108 Cases of Unilateral Loss of Vision*

Lesions	Cases	
	No.	Per Cent
Retrobulbar neuritis	10	9.2
Syphilis	19	17.6
Pituitary tumor	19	17.6
Meningioma	15	13.9
Craniopharyngioma	4	3.7
Aneurysm	3	2.8
Tumors or arachnoiditis with papilledema	6	5.6
Undiagnosed chiasmal lesions	16	14.8
Miscellaneous lesions	16	14.8
Total	108	100.0

lamic nuclei no longer can be considered benign, despite its histopathologic appearance.

SYMPTOMS AND DIAGNOSIS

Certain findings must be emphasized as aids to diagnosis of these meningiomas. For instance, 39 of the 52 patients who had meningiomas of the anterior clinoid process were females. This preponderance of females has been noted by other authors.[1] It leads to interesting speculations as to the influence of hormones in the development of these meningiomas.

1. Cushing, H., and Eisenhardt, L.: Meningiomas: Their Classification, Regional Behaviour, Life History, and Surgical End Results, Springfield, Ill., Charles C Thomas, Publisher, 1938. Grant, F. C.: Intracranial Meningiomas: Surgical Results, Surg., Gynec. & Obst. **85**:419-431 (Oct.) 1947.

The symptoms of four of the patients began or were accentuated during pregnancy; the symptoms of three others began in the postpartum period. In a recent study of 10 other patients seen at the clinic, it was observed that pregnancy may exert a marked effect on meningiomas.[2] In view of this observation, the importance of careful evaluation of loss of vision occurring during pregnancy or the postpartum period should be recognized.

The average age of the patients at the time of diagnosis was 45 years. The youngest patient was 14. He had been blind in the left eye since the age of 6 years. A cellular meningothelial meningioma, weighing 200 gm., was removed completely. The oldest patient was 62.

In 30 of the 52 cases the initial symptom was loss of vision; in 4 cases convulsive seizures were the initial symptom. Other symptoms which seemed to herald the onset of difficulty arising from the tumor were puffiness of one eyelid, anosmia, mental change, photophobia, diplopia, episodes of giddiness, and weakness of the legs.

The average duration of symptoms before the diagnosis was made was 4 years; the shortest duration was 6 weeks, and the longest, 16 years.

Loss of Vision.—A history of loss of vision was obtained in 48 cases. In 30 cases this began as a unilateral defect and progressed to complete loss of useful vision in the eye concerned. In 15 of these 30 cases loss of vision also occurred in the other eye, usually causing the patient to seek medical attention again.

Headache.—Headache occurred in 40 cases. It was often described as retro-orbital. Nausea and vomiting commonly were associated with the headache.

Other Symptoms.—Personality changes were frequent. Convulsive seizures were noted in 10 cases. An interesting symptom noted by several patients was a rather rapid gain in weight. This, we feel, probably is due to dysfunction of the orbital surface of the frontal lobes or to hypothalamic compression.

General Examination.—Results of general physical examination usually were not significant. In 2 cases mild hypertension was found; in two others clinical evidence of anterior hypopituitarism was exhibited.

Neurologic Examination.—Results of neurologic examination, aside from the ophthalmologic findings, were normal in the majority of cases. However, a decrease in the sense of smell was found in 15 cases, and in most cases this decrease was unilateral. In 14 cases some evidence of a departure from normal in muscle reflexes or diminution of strength between the two sides of the body was exhibited.

Ophthalmologic Examination.—The most important single part of the physical diagnosis was examination of the eyes. Measurement with the exophthalmometer disclosed unilateral exophthalmos in 12 cases. The pupils were unequal in many cases. In most of the 30 patients with a blind eye, the pupil did not react to light by direct stimulation, but did react consensually. Paresis of the extraocular muscles was noted occasionally.

Results of ophthalmoscopic examination were considered normal in only five cases. Unilateral atrophy of the optic disk was the commonest ophthalmoscopic

2. Weyand, R. D.; MacCarty, C. S., and Wilson, R. B.: Effect of Pregnancy on Intracranial Meningiomas Occurring About the Optic Chiasm, S. Clin. North America **31**:1225-1233 (Aug.) 1951.

finding. In some cases it was accompanied by papilledema in the other eye (Kennedy's syndrome). Unilateral papilledema was the only ophthalmoscopic abnormality observed in three cases. Bilateral papilledema was present in seven cases. In the majority of these cases the papilledema was more pronounced on the side on which the tumor was situated. Bilateral optic nerve atrophy was observed in 10 cases.

Perimetric examination was performed in all the 52 cases, and the visual fields were found to be normal in only 2 cases. Complete loss of vision in one eye was observed in 30 cases. In 15 of these 30 cases both the vision and the perimetric field of the other eye were normal. In the 15 remaining cases perimetric measurements disclosed temporal or inferior altitudinal hemianopsia, or contraction of the visual field.

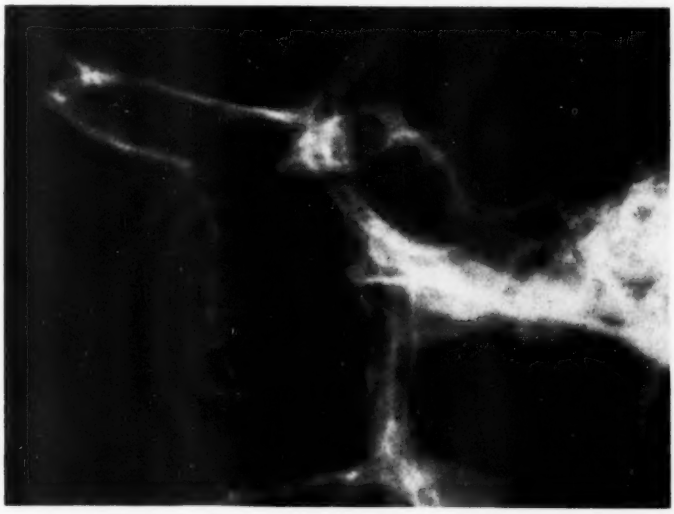

Fig. 2.—Osteoma in front of anterior clinoid process.

Unilateral central scotoma, contraction of the visual field, bitemporal hemianopsia, or homonymous hemianopsia was observed in a few cases.

Roentgenologic Examination.—The results of routine roentgenographic examination of the skull [3] suggested the presence of a tumor of the brain in 36 cases. Erosion of the sella turcica or the parasellar region was noted in 22 cases. In 14 cases the roentgenographic findings indicated the presence of an osteoma involving the anterior clinoid process and the surrounding structures (Fig. 2). In one case in which an osteoma was found at operation, roentgenographic examination dis-

3. Camp, J. D.: Osteoma of the Sphenoid Bone and Dural Endothelioma: Report of a Case, Am. J. Roentgenol. **11**:523-524 (June) 1924. Sosman, M. C., and Putnam, T. J.: Roentgenological Aspects of Brain Tumours: Meningiomas, ibid. **13**:1-10 (Jan.) 1925. Pendergrass, E. P.; Hope, J. W., and Perryman, C. R.: Roentgen Diagnosis of Meningiomas of Sphenoidal Ridge, Radiology **53**:675-706 (Nov.) 1949.

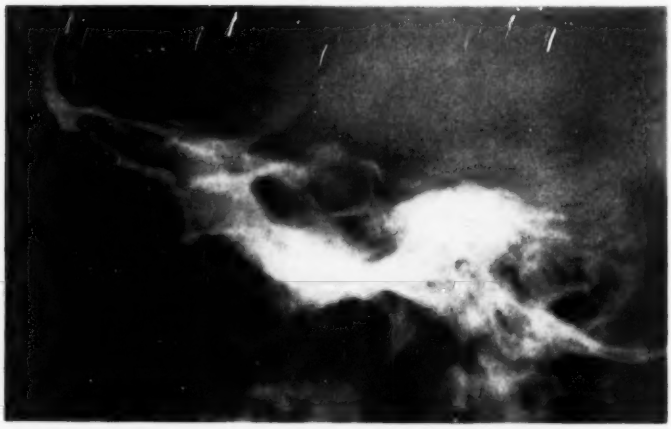

Fig. 3.—Calcified tumor surrounding anterior clinoid process.

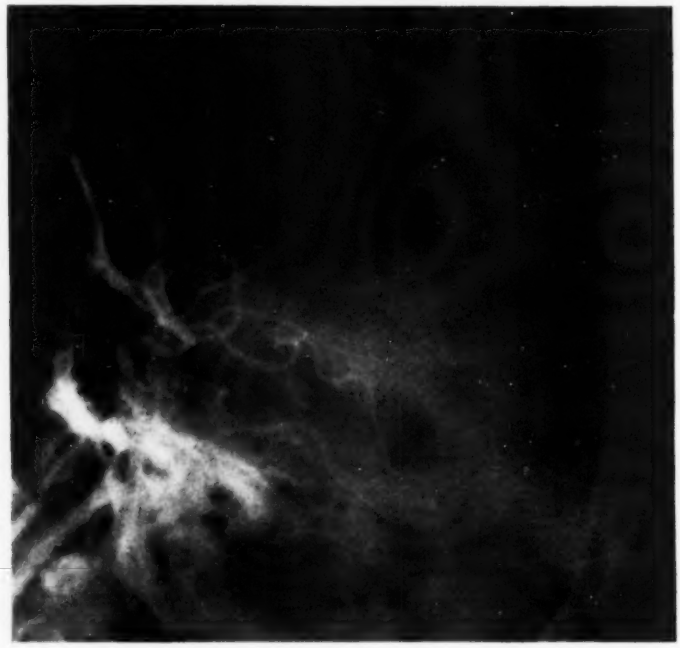

Fig. 4.—Angiogram of right internal carotid. The carotid siphon is straightened, depressed, and displaced posteriorly.

closed marked thickening of the sphenoid bone, which was regarded as an anatomic variant. In three cases a calcified tumor was observed in the roentgenogram (Fig. 3). Similar roentgenologic changes have been reported by other authors.

Other Diagnostic Procedures.—Electroencephalographic studies were made in 11 cases, in all of which the results were abnormal. Electroencephalograms were considered of localizing value in six cases.

The basal metabolic rate was determined in seven cases in which the history was suggestive of hypothyroidism. The rate was found to be less than —15% in four cases.

Lumbar puncture was performed in seven cases. In four cases the value for the cerebrospinal fluid protein was more than 60 mg. per cubic centimeter of fluid.

Ventriculographic studies were made in three cases, and a pneumoencephalographic examination was made in one case. In all the four cases these diagnostic procedures revealed evidence of a space-occupying lesion. Angiograms were made in three cases. In one case the angiogram was technically unsatisfactory, and in the other two cases the angiograms disclosed posterior displacement and straightening out of the carotid siphon (Fig. 4), findings which were considered diagnostic of a tumor.

TREATMENT

Treatment of meningiomas of the anterior clinoid process is always surgical, because prolonged delay will result in total blindness. Blindness precedes death from increased intracranial pressure by many years.

The anesthesia of choice for removal of meningiomas of the anterior clinoid process is ether administered by the open-drop method, with a Magill intratracheal tube. Recently, several operations have been carried out successfully by the intravenous administration of a 2.5% solution of thiopental (pentothal*) sodium containing curare and by the intratracheal administration of nitrous oxide and oxygen. Loss of blood, which at times is severe, is immediately remedied by the use of whole blood from the blood bank. The advantage of immediate replacement of fluid is immeasurable and is lifesaving in these patients. At the start of the operation, the insertion of a needle in the saphenous vein, through which a 5% solution of dextrose and water is permitted to drop slowly, will afford a readily available means of intravenous therapy. Arterial autoperfusion, as recommended by Gardner,[4] is helpful in controlling bleeding.

Improvements in surgical technique and in balanced anesthesia [5] and supportive therapy have made radical removal of these tumors possible. The surgeon usually prefers to approach the tumor on the side of the greater visual loss. A right or a left transfrontal osteoplastic craniotomy usually will afford adequate exposure. If there is evidence that the tumor may cross the midline, bilateral block removal of the frontal bone, with a Souttar scalp incision, should be employed. This permits bilateral exposure. After the bone flap has been reflected, use of the extradural approach to the wing of the sphenoid bone is recommended to protect the frontal

4. Gardner, W. J.: Control of Bleeding During Operation by Induced Hypotension, J. A. M. A. **132**:572-574 (Nov. 9) 1946.

5. Lundy, J. S.: Balanced Anesthesia, Minnesota Med. **9**:399-404 (July) 1926; Progress in Balanced Anesthesia, Journal-Lancet **51**:743-745 (Dec. 15) 1931.

lobe. The dura is opened along the wing of the sphenoid, and the incision is extended anteriorly toward the tip of the frontal lobe and curved upward toward the vertex of the skull. The dural opening is best extended posteriorly to expose the Sylvian vessels. Exposure of these vessels lessens the danger of compressing them when one is retracting the frontal lobe. The ipsilateral olfactory nerve may be unavoidably injured or destroyed to obtain exposure.

The tumor is exposed by elevation of the frontal lobe. If difficulty is encountered, it may be necessary to resect the tip of the lobe. The insertion of a brain cannula in the frontal horn of the lateral ventricle and removal of the ventricular fluid will reduce intracranial tension. An alternative is to place a spinal puncture needle or catheter in the lumbar subarachnoid space before craniotomy. Then, by means of a rubber tube and syringe attached to the needle or catheter, sufficient cerebrospinal fluid can be allowed to escape to decrease the intracranial pressure and thus facilitate exposure.

Meningiomas of the anterior clinoid process are very vascular, but, unlike meningiomas of the wing of the sphenoid bone, their blood supply cannot be reduced by ligation of the external carotid artery. Much of the blood supply of meningiomas of the anterior clinoid process seems to arise from the tuberculum sellae and from the lesser wing of the sphenoid bone. If the site of attachment of the tumor can be coagulated safely with the electrosurgical unit, much bleeding can be controlled thereby.

The tumors are best removed piecemeal with a small electrosurgical loop, as suggested by Cushing [6] in 1927, with excavation of the center of the tumor and peeling of the capsule inward to effect complete removal. After the core of the tumor has been removed, both optic nerves and the optic chiasm must be inspected carefully to insure that injury to those structures will be minimized when the remainder of the tumor is elevated. It may be found that the capsule of the tumor is supplied by small branches of the anterior cerebral artery. If so, these vessels should be isolated and coagulated, if possible. Should brisk bleeding ensue, a pledget of muscle may serve as a tampon to control the hemorrhage. If this is not successful, ligation of an anterior cerebral artery may be necessary, but it should be carried out only in the presence of a sustained systolic blood pressure.[7]

That part of the clinoid process to which the tumor is attached should be coagulated gently to destroy any arachnoid rests. If an osteoma is found, it should be removed with a rongeur, and bleeding should be controlled.

Drainage of the operative site is not necessary. Preferably, it should be avoided.

In six cases, two operations were required to remove all of the tumor, and in one of these cases the unilateral approach was abandoned in favor of the bilateral approach. In our series of 52 cases, the bilateral flap was used primarily to expose meningiomas on the left. In five cases additional operative procedures were required for evacuation of a blood clot (three cases), to accomplish temporal decompression (one case), and to combat wound infection (one case).

6. Cushing, H.: Meningiomas Arising from the Olfactory Groove and Their Removal by the Aid of Electro-Surgery, Lancet **1**:1329-1339 (June 25) 1927.

7. Poppen, J. L.: Ligation of the Left Anterior Cerebral Artery: Its Hazards and Means of Avoidance of Its Complications, Arch. Neurol. & Psychiat. **41**:495-503 (March) 1939.

PATHOLOGIC ASPECTS

The actual size of these tumors could not be measured accurately because they were removed piecemeal.

Histologically, most of these tumors were not malignant. Their ability, however, to surround vessels and nerves at the base of the brain makes complete surgical removal of them hazardous indeed, regardless of the relatively benign microscopic picture. The predominant tumor type was classified as a meningiothelial meningioma (Fig. 5). In a few cases, however, the tumor was of the fibroblastic, psammomatous, or angiomatous type.[8]

RESULTS

Among the 52 cases there were 17 postoperative deaths in the hospital, or a mortality rate of 32.7%. Death was caused by cerebral edema, after subtotal

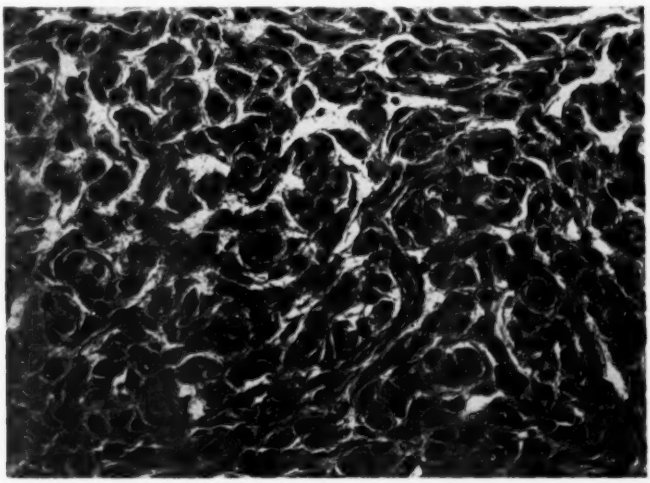

Fig. 5.—Meningothelial meningioma. Hematoxylin and eosin stain; × 200.

removal of a tumor, in 10 cases; by hemorrhage in 3 cases, and by thrombosis of either the anterior cerebral or the middle cerebral artery in 4 cases. Most of the deaths occurred before the eighth postoperative day.

An attempt was made to obtain follow-up data in the 35 cases in which the patients survived the operation. We were not able to reach three of the patients.

Of the 32 patients whose condition we were able to follow, 5 died between one year and seven years after operation, probably of recurrence of the tumor. Seventeen were well at the time of this report, and, although they had unilateral anosmia and decreased vision in one eye, they were able to read and work. Nine of these 17 patients had been well for more than six years. The 10 remaining patients, who were alive when last heard from, were unable to work because of mental impairment, hemiparesis, or blindness.

8. Bailey, P., and Bucy, P. C.: Origin and Nature of Meningeal Tumors, Am. J. Cancer **15**:15-54 (Jan.) 1931.

SUMMARY AND CONCLUSIONS

As Cushing[9] aptly said:

> Intracranial tumors are so protean in form; they behave in such different ways; they provide such varied clinical pictures, and the proper method of dealing with many of them, even when they are exposed by an operation, is in many cases so problematical, that our only hope for progress is to particularize on certain groups of cases.

Meningiomas of the anterior clinoid process grow slowly and are relatively silent. If early recognition is not urged and achieved, these tumors will grow to such a size before coming to the surgeon's attention that total removal will then be attended with much risk. Total removal of these tumors is necessary to prevent recurrence. We believe that early neurosurgical consultation, the making of stereolateral roentgenograms of the skull, and the accurate performance of tests of the visual fields are indicated in every case in which a patient complains of unilateral visual impairment. If this plan is followed, we believe that early diagnosis can be made and that the tumors can be removed rather easily, and with few complications and a comparatively low mortality rate, before irreparable loss of vision occurs.

9. Cushing, H.: The Meningiomas (Dural Endotheliomas): Their Source and Favoured Seats of Origin, Brain **45**:282-316 (Oct.) 1922.

DEPTH OF FOCUS AND AMPLITUDE OF ACCOMMODATION THROUGH TRIFOCAL GLASSES

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ST. LOUIS

MANY STUDIES have been made of the "amplitude of accommodation" in presbyopia, but there has been little attempt to measure its component parts. Since it is a complex of active accommodation, depth of focus, and interpretation or suppression of blur fringes, the old term should be changed to "range of clear vision."

Many textbooks contain figures for depth of focus of the human eye derived mathematically from the dimensions of a foveal cone, but to my knowledge there

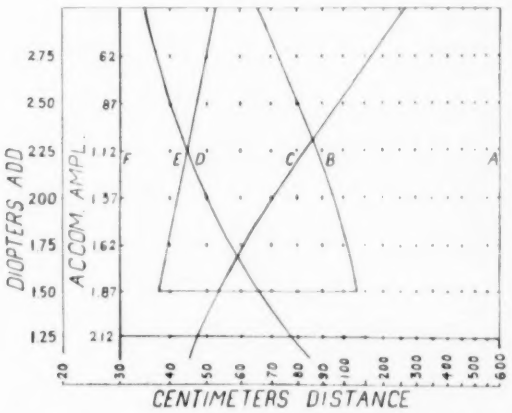

Fig. 1.—The range of clear vision through the distance portion of a trifocal lens should theoretically be from line *A* to *C*, according to the amplitudes of accommodation indicated. Through the intermediate addition, vision should be clear from the reciprocal distance *B* to the accommodative near point *E*. Likewise for near, vision should be clear from line *D* to *F*.

are no subjective data except those of Ogle [1] (1927) and Burian and Schubert [2] (1936). They used the same method and obtained results similar to those to be described here.

From the Department of Ophthalmology and the Oscar Johnson Institute of the Washington University School of Medicine.

Read before the Section on Ophthalmology at the One Hundred First Annual Session of the American Medical Association, Chicago, June 11, 1952.

1. Ogle, K. N.: Measurement of the Depth of Focus of Human Eyes, Thesis, Dartmouth College, 1927.

2. Burian, H., and Shubert, G.: Das Wesen der Naheeinstellungs-Reaktion der Pupillen, von Graefes Arch. Ophth. **136**:377-386, 1936.

In the present study, measurements of range of clear vision on test type, depth of focus, and irreducible accommodative tone of 25 private patients were taken at distances of 40, 80, and 600 cm. through appropriate portions of trifocal lenses. Considerable differences from the usual theoretical presentation of ranges of clear vision through trifocal lenses (Fig. 1) were found.

PROCEDURE

Ranges of clear vision were tested binocularly through the new trifocal glasses on a reduced Snellen test chart designed for use at 40 and at 80 cm. To obviate the effect on retinal image size of moving the chart nearer the eyes, I requested the patient to keep shifting his gaze to the smallest letters easily visible. While my right hand kept the zero end of a meter stick against the outer canthus of the patient's left eye, my left hand could move the test chart freely along the stick. The results of these tests are shown in Figure 2.

The part of the range of clear vision due to depth of focus of the eye can easily and precisely be measured by the stigmatometer (Fig. 3). This instrument is a modification of the refracting optometer, in which all eyes are made myopic by a strong plus lens, say 10.00 D. A point target may slide freely along the visual line so that the patient can move it to the artificial myopic far point. If the test object blurred at a distance of 10 cm. (10 D.), the refraction of the patient was 10 minus 10, or emmetropia. If the distance became 5 cm. (20 D.), the refraction was 10 minus 20, or −10.00 D. A distance of 20 cm. would indicate +5.00 D. of hypermetropia.

When an optometer is placed on each side arm of a Tschermak haploscope,[3] the result is a stigmatometer,[4] my modification of which is illustrated here.[5] With this instrument, both the patient's eyes can be fixing on a target while the conjugate focus of a point on the fovea is determined for either eye independently. The level of accommodation of an eye can be measured with fixation and convergence controlled at any distance.

Figure 3 shows that this stigmatometer is attached to the space eikonometer, which is used merely as a head holder for perfect alignment of the eyes. The attached side arm shows the distance equivalent scale, which is interchangeable with the scale in diopters. The other side arm is lying on the table to show the patient's control knob. The side arms slide on the front arc support in convergence, permitting rotation of the visual line for the side arm in the horizontal plane through the ocular rotation center. In effect, both eyes can observe a Snellen test chart at any distance, while superimposed on the center of the chart is a point of light which can be moved along the visual line of one eye from the plane of the binocular target back into the distance, or nearer the eye, until it appears sharp. Its position in space can be measured precisely and shows the level of accommodation an eye will take under fixed conditions, which is seldom exactly on the point of binocular fixation.

Between the target light and the plate glass used as a semitransparent mirror, and 25 cm. from the eye, is the + 4.00 D. lens, which condenses all distance between 20 and 1,000 cm. into a convenient 22-cm. scale. The light-point target consists of a knife-edged 0.05 mm. aperture before a diffusing disc and a 2.5-volt AC dial lamp, operated by the toggle switch on the base of the eikonometer.

With the patient's prescription for near in the eikonometer lens holders, the instrument was aligned to the proper vertex distance and visual lines. First, the side arms were converged for a binocular fixation distance of 40 cm. The patient observed the light point superimposed on a well-illuminated reduced Snellen chart near the "20/20" line, at 40 cm. The patient was asked to pay attention to the test type while focusing the bright point. Any tendency of the eyes to accommodate for the stigmatoscope light instead of the test type is apparently prevented by the excellent distance certainty of binocular vision.

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3. Herzau, W.: Über das Verhältnis von erzwungener Vertikaldivergenz und Rollung bei der Fusion, von Graefes Arch. Ophth. **122**:59-74, 1929.

4. Bannon, R. E., and others: The Stigmatoscopy Method of Determining the Binocular Refractive Status, Am. J. Optom. **27**:371-384, 1950.

5. Made by William F. Fuchs, of Washington University Mechanical Shop, by aid of a grant from the Univis Lens Company.

With the right-side target lighted, the patient was shown the effect of turning the knob from blur to sharp to blur. He was instructed to try to leave the setting halfway between equal blurs. Three such readings varied less than 2 cm. on the side-arm scale, corresponding to an accommodative change of less than 0.12 D. The accommodative level being obtained, the depth

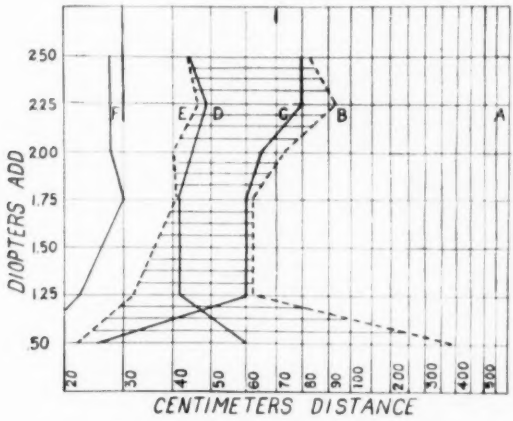

Fig. 2.—Average ranges of clear vision for 17 presbyopic patients measured on test type through trifocal glasses.

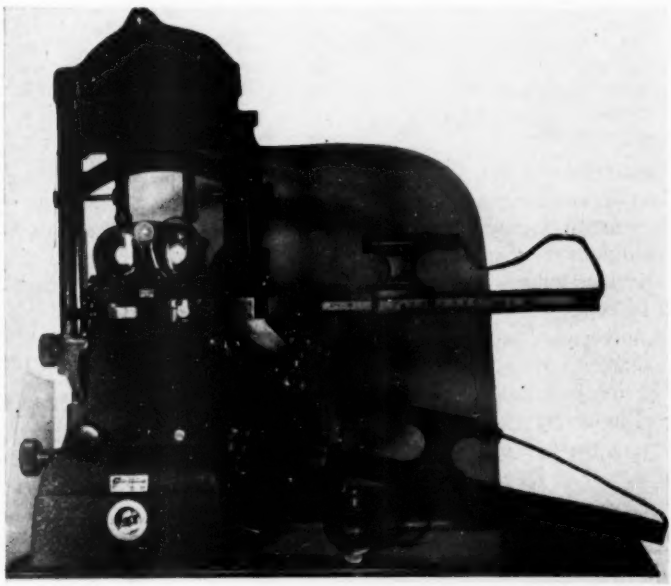

Fig. 3.—Modified haploscope used for measuring level of accommodative tone and depth of focus by stigmatoscopy. In use, both side arms are kept symmetrically attached to the head holder.

of focus was measured by movements of the target rider by the examiner in either direction until the patient reported a blur. Records were kept of the best average focus and the average depth of focus of the light point in front of and behind the binocular target.

This procedure was repeated for the left eye; then the side arms were converged for 80 cm., and the reading addition in the lens holders was reduced one-half. Then the best conjugate focus for the Snellen chart at 80 cm. and the depth of focus before and behind were measured as before.

Finally, tests were repeated with convergence and refractive correction for the Snellen chart at 6 meters' distance.

RESULTS

Results for the 25 presbyopic patients were averaged according to the reading addition and are represented graphically in Figure 4. The three straight lines, *A*, *B*, and *C*, show the positions of binocular test chart fixation at distances of 40, 80, and 600 cm. The irregular triplet lines represent best conjugate foci, *A'*, *B'*, and *C'*. The outer lines of each triplet represent the limits of the depth of focus in front of and behind the conjugate focus. While both eyes look at *A*, they focus at *A'*, which is nearer. Point objects within the depth limits would appear sharp, all others would be blurred. Larger objects, even test type, would show greater depth of focus. Colored objects should show the same depth of focus, but a different position.

Depth of Focus of the Eye, Expressed in Diopters, at 40, 80, and 600 cm., Showing the Range of Variation in This Series of Patients

Reading Addition, D.	No. of Eyes	Near, D.			Intermediate, D.			Distance, D.		
		Low	Average	High	Low	Average	High	Low	Average	High
+2.50	14	0.14	0.31	0.63	0.06	0.28	0.57	0.13	0.23	0.38
+2.25	8	0.12	0.31	0.43	0.06	0.17	0.24	0.08	0.37	1.04
+2.00	8	0.25	0.56	1.12	0.11	0.32	0.69	0.10	0.30	0.84
+1.75	6	0.31	0.65	1.16	0.27	0.55	0.93	0.10	0.39	0.66
+1.50	2	0.19	0.20	0.22	0.10	0.17	0.24	0.14	0.15	0.17
+1.25	6	0.14	0.29	0.48	0.06	0.06	0.13	0.24	0.09	0.36
+0.50	6	0.31	0.58	1.10	0.10	0.18	0.37	0.09	0.18	0.31
Average			0.40			0.26			0.26	

The depth-of-focus figures in the accompanying Table show fairly good uniformity and precision considering the type of subjects used. Of 28 patients tested, only 3 gave totally inconsistent data, not used. An increased depth of focus with stronger additions does appear in Figure 4, but it is considered due to increased tolerance for blur fringes in older presbyopes. The pupillary size in each case was estimated by comparison with a standard; and when plotted against depth of focus it showed no correlation.

Accommodative miosis appeared to increase the depth of focus in this group, but here, again, the data are misleading. Owing to the nature of the test instrument, the point of light target appeared larger in near vision than at distance. In the 12 best observers, the figures showed a depth of focus of 0.46 D. at a 40-cm. distance, compared with 0.31 D. at 80 cm. and 0.19 D. at 6 meters.

The construction in Figure 5 is different from Figure 1 in that the lines designate distances within which prolonged visual work on very small objects should remain comfortable. Such should be the practical consideration in the design of trifocal glasses.

In the average presbyopic patient who has a habitual reading distance of 40 cm. (16 in.), the addition should be enough to bring his momentary clear vision limit to 28 cm. (Fig. 5, line *G*). Vision at the 40-cm. line makes use of available accommodation and depth of focus. The latter is known for the stigmatoscopy target; so

from line *H* back to line *I*, no accommodation is required. The far blur point through the reading addition, line *E*, is constructed from the reciprocal of the addition dioptric power, as in Figure 1. This line corresponds in accommodative level to line *A*, or infinite distance, optically. It is evident from Figure 2 that the far blur point

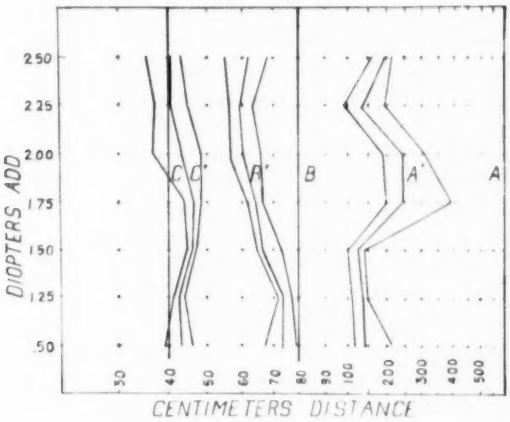

Fig. 4.—Stigmatoscopic findings in 25 presbyopic patients who were observing test type binocularly through trifocal lens powers appropriate for distances of 40, 80, and 600 cm. The central line of each triplet indicates best conjugate-focus distance, while the other two indicate depth of focus.

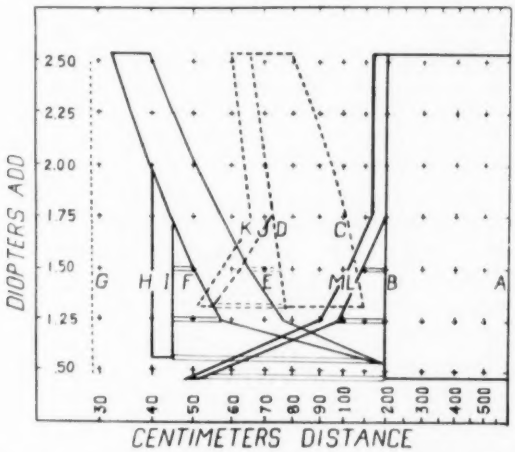

Fig. 5.—An estimate of ranges of clear comfortable visual work on small objects which could be maintained for prolonged periods through trifocal spectacle lenses. Only the portions marked in paired horizontal lines require active accommodation. Depth of focus and irreducible accommodative tone account for most distances.

is more proximal. The difference may be due to irreducible ciliary tone. This quantity was measured with the greatest sensitivity and repeatability at 600 cm. and is recorded as line *A'* in Figure 4. It apparently does not vary with age or reading addition. In normal subjects, while binocular fixation is at distance, the eyes actually

focus at about 2-meter distance, which is 0.50 D. nearer.[6] If this degree of accommodative tone cannot be reduced in distance fixation, it certainly is not to be reduced in any near-vision distance. Therefore, in Figure 5, 0.50 D. is taken from the far end of each of the three ranges of comfortable vision, to represent distances of vision in which no effortful accommodation is required. The difference from line *F* to line *I* is the remaining range of distance in which active accommodation must be used, and is marked in horizontal paired lines.

The components of the intermediate and distance ranges of comfortable vision were plotted in Figure 5, from similar reasoning. Even though 1 D. of accommodation is held in reserve for comfort in this figure, and it is assumed that prolonged visual work on small objects is to be done, the relative amount of active accommodation required is surprisingly small.

COMMENT

Measurements of the range of clear vision on test types could be improved by any device which could produce a constant visual angle and brightness contrast at various visual distances. However, the presbyopic patient, whatever his occupation, may develop a tolerance to blur and poor contrast, so that experimental results might not be greatly different from those reported here. Such adaptation to presbyopia may explain the tendency of some patients to reject full correction. Patients who wear glasses only part time may prefer a blurred image at both distance and near. On the other hand, those habituated to glasses may complain of a 0.12-D. error.

This study has shown the importance of depth of focus, the state of ciliary tone, and the tolerance to blurred imagery in presbyopia. Even in early stages, active accommodation is unimportant, or is not much used. It has long been accepted practice to give + 0.50 D. "rest glasses" to emmetropic students complaining of reading difficulties. No one would hesitate to change the glasses in a patient wearing a reading addition of + 1.25 D. if vision is much better at the same distance with + 1.75 D. Why do we so seldom prescribe a + 0.50 D. addition in early presbyopia with the same handicap? Our practice in this regard has resulted in gradual loss of pleasure in reading in the evenings, or in a loss of work efficiency in our patients. It also has resulted in needless difficulty in learning to use bifocal glasses, when the first reading addition has to be + 1.50 D.

The same reasoning applies for vision in the 80-cm. distance range. An intermediate segment of + 0.62 D. proved very useful in a group of six early presbyopes associated with me in the medical sciences.[7] All continue to wear the trifocal glasses after two years and prefer them to bifocals. In other occupational groups, it would seem more reasonable to prescribe an addition of + 0.75 D. in the first glasses and then + 1.50 D. trifocals when indicated.

6. Ames, A., Jr., and Gliddon, G. H.: Ocular Measurements, Tr. Sect. Ophth. A. M. A., pp. 102-168, 1928. Ogle, K. N., and others: Repeatability of Ophthalmoeikonometer Measurements, Arch. Ophth. **24**:1179, 1940. Luckiesh, M., and Moss, F. K.: Functions of Relative Accommodation, Am. J. Ophth. **24**:423-428, 1941. Sheard, C.: Dynamic Skiametry and Methods of Testing the Accommodation and Convergence of the Eyes, in the American Encyclopedia of Ophthalmology, Chicago, Cleveland Press, 1920.

7. Miles, P. W.: An Experiment in Which 50 Presbyopes Were Provided with Trifocal Glasses, A. M. A. Arch. Ophth. **46**:542-548, 1951.

The lines of dashes in Figure 5 show that an intermediate segment 50% of the reading-addition strength is correct for a distance of 70 to 80 cm. Lenses are available with slightly different ratios for those whose occupation calls for a different intermediate working distance. A large variety of segment sizes and locations are also available. The one-piece trifocal may interfere with view of the ground in walking and, by the excess arc of segment superiorly, with distance gaze, but is useful to a secretary who looks through the large intermediate lens far to one corner of her desk.

The fact that the near limit of comfort indicated in Figure 5 is nearer than 40 cm. with the + 2.25 and + 2.50 D. additions would suggest that these powers should be reserved for persons who must work at distances less than 40 cm., for persons with esophoria at near, or for persons who need magnification because of reduced visual acuity. Tests for reading addition and for heterophoria at near may best be made by use of a trial set of bifocal lenses to fit the rear cell of the trial frame. The reduced addition requirement in the reading position of gaze as compared with that for straight ahead is then compensated, and also the common difference in heterophoria.

It has been said [8] that the state of heterophoria for near should be considered important in the determination of reading addition. Excess accommodative convergence may be a cause of esophoria and could be reduced by greater reading addition. In a few cases with exophoria, undercorrection for near can be useful to stimulate accommodative convergence. This is less successful in presbyopia, because accommodation may not follow excess stimulation. A sharp retinal image may be most important in heterophoria because it increases fusional amplitudes, which, in turn, overcome heterophoria.

Asthenopia is seldom due to insufficient accommodation in presbyopia. Blurred images are well tolerated. There is considerable doubt whether the ciliary muscle is subject to fatigue, since it is smooth muscle. On the other hand, asthenopia can frequently be attributed to poor fusion, natural or induced heterophoria, and cannot be relieved by reducing the accommodation alone. Patients having difficulty in wearing bifocal glasses do not complain of blur, except possibly in vision through the segment margin. What seems to bother many of them is the suddenly reduced necessity to converge in looking down through the reading addition. Too much exophoria from reduction of accommodative-convergence habits proves a burden to fusion.

The trouble caused the patient by our common tendency to prescribe too much reading addition power is not so much from blurring as from induced heterophoria. Any normal, nonpresbyopic person can wear a reading addition of + 2.25 D. if it is accompanied by prism. Some modern stereoscopes for 35-mm. kodachrome® film have a reading addition of 10.00 D. Scheffler [8a] prescribed lenses for presbyopic patients which incorporated 1 meter-angle of base-in prism per diopter of reading addition. The trifocal lens reduces this shock due to the induced heterophoria from the segment to two easy steps; this explains the clinical experience that patients find trifocals easier than bifocals to "break in."

8. (*a*) Scheffler; cited by Hartridge, G.: The Refraction of the Eye, Ed. 14, Philadelphia, The Blakiston Company, 1907, p. 194. (*b*) Hartmann, E.: Hétérophorie et changement de verres ou de l'advantage d'avoir parfois de mauvais verres, Ann ocul. **182**:57, 1949.

It should not be assumed that the zones outside those called comfortable in Figure 5 are visually useless. One might as well say that the peripheral visual field is visually useless. The blurred zones are seldom noticed by most people; they result in inconvenience, inefficiency, and gestures of the head in focusing, but not in discomfort.

SUMMARY AND CONCLUSIONS

The ranges of clear vision through multifocal glasses are derived from (1) effort-free accommodative tone, (2) true active accommodation, (3) depth of focus, and (4) suppression of blur fringes. These factors were studied by two methods: blur limits of vision on test types, and stigmatometry. The distance of conjugate focus of each eye of 25 presbyopic patients was measured through trifocal lens powers for binocular vision on test type at distances of 40, 80, and 600 cm. At the same time, the depth of focus on a point of light target was measured for each eye at the three distances.

The results showed that active accommodation is less important for clear comfortable vision in presbyopia than was formerly believed.

Reading additions of + 2.50 D. or more should be prescribed only when the reading distance is less than 40 cm., when there is esophoria, or when magnification would help poor visual acuity. Asthenopia is less frequently due to accommodative errors than to heterophoria introduced by multifocal lens segments. Determinations of reading addition and near heterophoria are more exact and physiological when done through bifocal trial lenses in the rear cell of the trial frame.

Since a patient who is wearing a + 1.25 D. addition but needs + 1.75 D. is advised to get new glasses, we should grant the same benefit in early presbyopia when the requirement is only + 0.75 D. The same reasoning applies to vision in the intermediate distance, which requires less addition than that in the reading position.

ABSTRACT OF DISCUSSION

Dr. Edwin Forbes Tait, Norristown, Pa.: The subject of Dr. Miles's very helpful paper is an extremely important one in the everyday practice of the average ophthalmologist.

It is certainly true that a full range of clear vision is greatly to be desired in cases of presbyopia, and the availability in recent years of multifocal lenses has made it possible to give sharp vision at practically every distance, from the most remote to the desired near point.

In the formulation of a lens prescription, the correction for distance and that for the reading point offer few difficulties, but there may be some question as to the desirable intermediate added power. In his paper, Dr. Miles has studied the extent to which clear vision is possible with each of the three lens components and has shown that there is, in general, an approximation or an overlapping of these clear vision fields when the intermediate addition is one-half the addition for near. I have had no experience with binocular stigmatoscopy but have used an optometer and many types of near-point tests including monocular stigmatoscopy, in experiments upon accommodation. From this experience, Dr. Miles's results, and other experimental reports included in the references in his paper, it would seem that the response of accommodation to nearness, which one may call the "proximal accommodative reflex," would have to be considered. In my experience, most, but not all, patients will accommodate to some extent when an object is close to the eyes, even though the fixation distance is compensated for by suitable lenses

and convergence relieved by a haploscope or prisms. It is this factor which may serve to explain the apparent 0.50 D. of accommodation for distance fixation which Dr Miles attributed to irreducible tone of the ciliary muscle.

There is, undoubtedly, in all normal persons who are not completely presbyopic a small, but constant, amount of accommodation which is due to the normal tonus of the ciliary muscle, and the innervation to the ciliary muscle for accommodation is probably present as long as life lasts. The amount of accommodation contributed to the eye by this tonus, however, must be considered as one component of the basic refractive condition; that is, a person who is emmetropic in the sense that he neither accepts nor requires glasses has actually a hyperopia of an amount equal to that of his tonic accommodation. Proximal stimuli, such as the semitransparent mirror and the other elements of the Tschermak haploscope used in this experiment, could encourage accommodative activity to the extent found by Dr. Miles, and it is this factor, combined with the long depth of focus always found in distance fixation, which may explain the lack of a subjective blur of test type at 6 meters when the apparent accommodation is for 2 meters.

Considerable experience in the prescription of trifocal lenses leads me to agree with Dr. Miles as to the desirability of prescribing them for persons requiring relatively low reading additions, depending, of course, upon the intelligence of the patient, his adaptability, and his visual needs. In my experience, reading additions of + 1.50 D. or more, with intermediate areas with one-half the addition, have been very useful in selected cases. On the other hand, regardless of the theoretical desirability of trifocals, there are some patients who cannot or will not accept them for constant wear. I have had, for instance, but moderate success with trifocal lenses in aphakic patients, with whom one would expect good results from the purely optical standpoint. The difficulty here, in many cases, seems to be that the reading addition, regardless of the type of construction of the trifocal, is too far in the periphery, producing unavoidable lens distortions, to which the patient objects.

I have not found that heterophoria at the near point, unless it be esophoria, is a factor in visual comfort either in bifocal or in trifocal prescriptions. In most cases, exophoria at the near point is simply a manifestation of the lack of accommodative convergence, which, in turn, is the result of a reflex system which functions only during fusional dissociation. The dominant and constantly used reflex system in binocular vision for near is that supplied by fusion, fusional vergence, which is independent of the heterophoria. Variations in the additions will make no difference in comfort in those persons whose distress is due to low fusional convergence amplitudes, in my experience the only procedures of value being base-in prisms or, preferably, fusional vergence training.

Esophoria at near is a factor to consider if it is present in presbyopic patients when wearing suitable correcting lenses. In early presbyopes it is almost always due to excessive accommodative convergence. This must be neutralized by divergent fusional effort, which usually results in convergence asthenopia. Excessive accommodation convergence is relatively rare in older presbyopes.

Convergence accommodation, a lack of which creates the lag of accommodation behind convergence to which Dr. Miles refers, is also a factor to be considered in prescribing either bifocals or trifocals to persons with early presbyopia if it is excessive. Fortunately, we do not encounter excessive convergence accommodation very often; so there is seldom any necessity for relieving the reflex by base-in prisms, though this, of course, can be done.

GLAUCOMA FOLLOWING OCCLUSION OF CENTRAL RETINAL ARTERY

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FORT LAUDERDALE, FLA.

A SEVERE form of secondary glaucoma, usually called hemorrhagic glaucoma, often follows occlusion of the central retinal vein. Occlusion of the central retinal artery has been reported to be followed by glaucoma in extremely rare instances.

The recent observation of two patients in whom sudden severe unilateral glaucoma developed a few weeks after an occlusion of the central retinal artery seems of sufficient importance to warrant the presentation of an analysis.

In 1927 Opin reported clinical and pathological observations on this condition.[1] A man aged 76, under treatment for mitral insufficiency and hypertension, lost the sight of his right eye suddenly and without pain. The characteristics of occlusion of the central retinal artery were seen ophthalmoscopically. No specific treatment was prescribed. Four and one-half weeks later the patient's right eye became painful. Intraocular tension was 40 mm. Hg. There were slight circumcorneal injection and epithelial edema. Physostigmine drops in the eye gave no relief during the following 10 days, and an enucleation was then performed. The left eye remained normal for the next five years of observation.

Microscopic examination of the globe was reported as showing occlusion of the central artery, just posterior to the lamina cribrosa, by an amorphous polygonal mass in the lumen of the vessel. The adjacent central vein was partially occluded by a recent thrombus, supposedly the result of stagnation of blood flow. The inner layers of the retina were the site of edema and degeneration. There was some congestion of the choroidal vascular bed. In the anterior segment, the iris root was seen to be adherent to the corneoscleral trabeculum, and on the anterior surface of the iris an endothelial proliferation had begun to form a fibrovascular membrane.

Opin further stated that he had previously examined 11 such eyes enucleated because of inflammatory glaucoma that followed occlusion of the central retinal artery.

In 1930 Bussola [2] reported a very similar case. His patient, an Italian merchant aged 54, had moderate hypertension and exertional dyspnea. Sudden blindness of the left eye occurred as the result of occlusion of the central retinal artery, diagnosed ophthalmoscopically. Six weeks later the blind eye became suddenly painful. There were ciliary injection, edema of the corneal epithelium, and congestion of the iris, with small hemorrhages in its ciliary portion. The immobile pupil was in mid-dilation; the intraocular tension was 60 mm. Hg (Schiøtz). Use of miotics resulted in no relief of pain or reduction of tension, and the eye was enucleated. The right eye was perfectly normal.

Pathological examination of the eye showed a noncellular mass filling the lumen of the central artery behind the lamina cribrosa and a coagulum in the central vein. The retina showed degeneration of the inner layers. The vascular network of the iris, ciliary body, and choroid was engorged, and there were small hemorrhagic extravasations in the peripheral portion of the iris. The filtration angle of the anterior chamber and the trabecular spaces were occluded by cellular proliferation.

From the Department of Ophthalmology, Emory University School of Medicine, and the Clay Memorial Eye Clinic, Grady Memorial Hospital, Atlanta, Ga.

1. Opin: Embolie de l'artère centrale de la rétine et glaucome secondaire (Examen anatomique), Arch. d'opth. **44**:321-341, 1927.

2. Bussola, E.: Embolia dell'arteria centrale della retina e glaucoma secondario, Boll. ocul. **9**:495-512, 1930.

Since 1930 there have been no reports of this condition, and the current textbooks seldom make mention of it. Duke-Elder,[3] in his discussion of occlusion of the central retinal artery, stated that "a secondary glaucoma has rarely occurred; in some cases it has been due to inflammatory and neovascular changes at the filtration angle, and in others it has been associated with co-existent venous thrombosis." No specific references are given. Under the heading of secondary glaucoma following occlusion of the central retinal vein, Sommers[4] stated that glaucoma is due to changes in the iridocorneal angle and that "similar causes may produce secondary glaucoma in obstruction of the central artery."

REPORT OF CASES

The following cases emphasize the features of this condition.

CASE 1.—N. T., a Negro woman aged 73, came to the Clay Memorial Eye Clinic on May 10, 1951, because her right eye had become blind suddenly during the previous week. In the past few years her visual acuity had been 20/50 in each eye. Retinal arteriolar sclerosis, Grade 2, was present, and the systemic blood pressure was 210/90. Mild diabetes mellitus was adequately controlled with insulin and diet. On two previous occasions the intraocular tension was recorded as normal to finger palpation in both eyes.

Visual acuity at the time of admission was limited to light perception in the lower temporal field of the right eye and was 20/50 in the left eye. Tension was measured as 20 mm. Hg in both eyes. Perimacular edema, a central cherry-red spot, and extreme narrowing of the retinal arterioles of the right eye were seen with the ophthalmoscope.

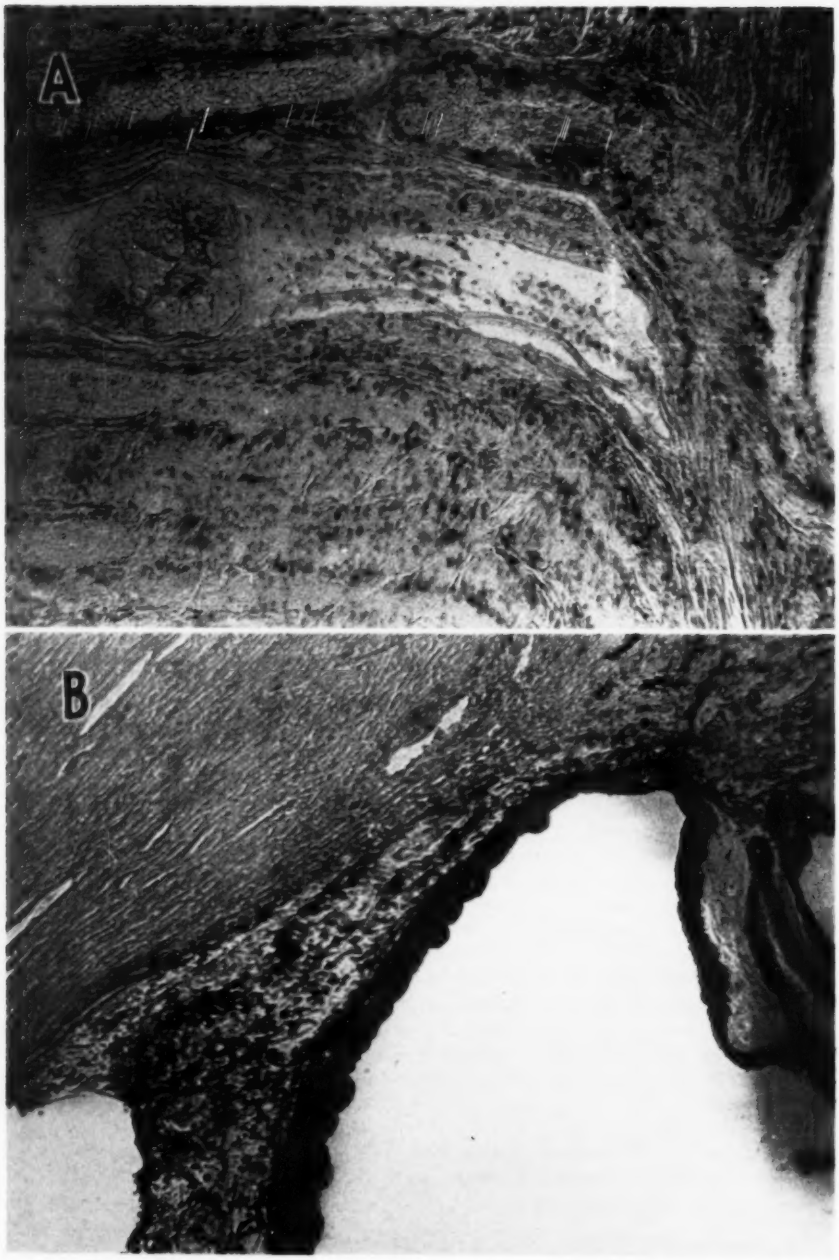
Ten weeks later, on July 19, the right eye, which by that time was totally blind, suddenly became extremely painful. There were corneal edema, superficial blood vessels, and free blood on the anterior surface of the iris, and the ocular tension was greatly increased. The anterior chamber was moderately shallow; the pupil was of average size and did not respond to light. Instillation of diisopropyl fluorophosphate solution, 0.1%, caused the tension to drop to 33 mm. Hg (Schiøtz) for one day, after which it rose to an unmeasurable height. Because of continued pain, the eye was enucleated on July 21. Tension in the left eye has remained normal during the past five months of observation. A combined water and mydriasis provocative test showed no tendency toward glaucoma in this eye. Gonioscopic study revealed an angle of normal depth.

Pathological examination of the enucleated right eye confirmed the clinical picture. The central retinal artery, just posterior to the lamina cribrosa, was completely occluded by a rounded, noncellular mass, showing slight calcification (Figure, *A*). This was interpreted as an embolus from an atheromatous plaque in a larger artery, nearer the heart. The adjacent central retinal vein showed round-cell infiltration of the adventitia, probably a periphlebitis secondary to the arterial block. The retina showed conspicuous loss of ganglion cells and some edema of Henle's fiber layer in the perimacular area.

There was some edema of the corneal epithelium. The periphery of the iris was adherent to the corneoscleral trabeculum on both sides (Figure, *B*). A mass of new tissue was seen between the iris and the cornea. It consisted of epithelioid cells and small blood vessels. Since the increased intraocular tension had been present only 48 hours before enucleation, it is not certain whether this tissue in the angle represents a very early membrane that would have spread along the iris surface or an early synechia of unusual character. In the two cases referred to above the changes were no more extensive than in this, even though ocular hypertension had persisted for a slightly longer period. There was no vascular congestion of the ciliary body and processes in the present specimen.

3. Duke-Elder, W. S.: Text-Book of Ophthalmology, Vol. 3, St. Louis, C. V. Mosby Company, 1940, p. 2566.

4. Sommers, I. G.: Histology and Histopathology of the Eye and Its Adnexa, New York, Grune & Stratton, Inc., 1949, p. 698.



A, embolus in the central retinal artery; *B*, fibrovascular synechia in the iridocorneal angle.

CASE 2.—S. W., a Negro aged 49, first came to the Clay Memorial Eye Clinic on Nov. 6, 1951, complaining of fluctuating, but progressive, loss of vision in the right eye during the previous five days. There had been no pain in either eye and no episodes of a similar nature in the past.

Visual acuity was 5/200 in the right eye and 20/25 in the left eye. External inspection revealed no abnormalities. The intraocular tension was normal in both eyes as estimated by finger palpation. Ophthalmoscopic examination revealed the presence of hypertensive arteriolar sclerosis, Grade 2. In the right eye there was a large circular area of edema in the perimacular region. The smaller retinal vessels were not visible in the posterior pole, but all the larger arterioles and the central artery seemed equal in size to those of the left eye (about one-half to two-thirds normal size). The macula appeared as a dull-red spot in the center of the whitish area. This condition was interpreted as either a central angiospastic retinopathy or a temporary occlusion of the central retinal artery with residual perimacular edema.

The blood pressure in the brachial artery was 190/120 mm. Hg. The fasting blood sugar was 87 mg. per 100 cc.

During the next week, the central artery and its branches in the right eye became steadily narrower, and visual acuity decreased to the point of mere light perception. By Dec. 6 it was felt that a diagnosis of occlusion of the central retinal artery was justified. Throughout this period the intraocular tension remained normal in both eyes (finger palpation test).

On Dec. 13 the patient returned to the clinic complaining of pain in the right eye, which was then totally blind. Intraocular tension was 72 mm. Hg (Schiøtz) in the right eye and 20 mm. Hg in the left eye. There was epithelial edema of the right cornea. After instillation of glycerin, the cornea cleared enough to permit further study of the intraocular structures. The anterior chamber was of average depth; the pupillary diameter was 3 mm. The fundus appeared as previously described. The frequent use of physostigmine ointment for the next 24 hours failed to reduce the intraocular tension below 62 mm. Hg. An ab externo iridectomy was then performed on the right eye. After operation the eye became free of pain, although the tension remained between 40 and 50 mm. Hg (Schiøtz). The iris surface was smooth and atrophic, and there was moderate ectropion of the pigment epithelium at the pupillary margin. On gonioscopic examination, the iris was seen to be adherent to the cornea in such a manner as to cover the trabeculum. The iridocorneal angle of the left eye appeared normal.

A water provocative test failed to produce an abnormal rise in the pressure of the left eye.

The clinical features seen in these cases of glaucoma following occlusion of the central retinal artery parallel in many aspects those of glaucoma following occlusion of the central vein and may be summarized as follows:

Complete or incomplete interruption of the arterial circulation of the retina occurs in a patient of middle age or beyond who has evidence of generalized vascular disease. After a quiet interval of 4½ to 10 weeks, sudden severe, painful glaucoma develops in the blind eye. The pupil is normal in size or slightly dilated. Miotic therapy appears not to result in any prolonged reduction of intraocular tension or relief of pain. Small blood vessels become visible on the anterior surface of the iris. Gonioscopic study at this stage shows the filtration angle to be occluded by a peripheral anterior synechia. Microscopically, a fibrovascular membrane joining the iris root to the trabecular portion of the cornea can be identified. Edema of the corneal epithelium and bullous keratitis develop if the tension remains high.

The eventual outcome is usually enucleation, but in one case, in which neovascularization of the iris was not present, an ab externo iridectomy was successfully performed and gave relief of pain. Cyclodiathermy is another procedure that may be tried in some cases.

The glaucoma that follows occlusion of the central retinal artery appears to be a definite secondary glaucoma and not a coincidental attack of primary glaucoma. In not one of the patients with this condition did glaucoma develop in the other eye, nor could a tendency toward glaucoma be demonstrated by provocative tests in the two patients reported here.

The pathological studies reported here do not clarify the pathogenesis of this form of glaucoma, but all three globes showed similar changes, suggesting that a common mechanism produced the intractable glaucoma.

SUMMARY

Two cases are presented in which a sudden severe unilateral glaucoma developed 4½ to 10 weeks after occlusion of the central retinal artery in the affected eye. Pathological findings in the one eye that was enucleated are described. A fibrovascular peripheral anterior synechia, similar to, but less extensive than, that found in hemorrhagic glaucoma following occlusion of the central retinal vein is found in the iridocorneal angle. This clinical picture is of extremely rare occurrence, but the remarkably consistent findings in these cases and in previously reported ones should justify its being included with the secondary glaucomas.

15 S.E. 16th St.

HISTOLOGIC APPEARANCE OF AN EYE FOUR DAYS AFTER CATARACT EXTRACTION

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IT IS ONLY on rare occasions that one is afforded an opportunity for the histologic study of an eye removed very soon after operation, particularly cataract extraction. Concepts of ocular wound healing are based mainly on studies of animal eyes,[1] recently summarized by Dunnington.[2] The healing process in cataract incisions begins anteriorly and proceeds posteriorly. Wounds covered by a conjunctival flap are first sealed by a fibrovascular plug from the surrounding episclera, the plug filling the outer half of the incision by the end of the second day; proliferation of endothelium begins after the fifth day. In the absence of a flap, corneal epithelium surrounding the incision proliferates to form a plug, which first bridges the anterior surface and then extends into the lips of the wound. Healing is firm in 10 to 12 days and is supposedly complete by the end of the 3d week. Abnormalities in wound closure are overlapping, anterior gaping, and posterior gaping. Improper placement of sutures may predispose to any of these abnormalities. Superficial sutures may result in posterior gaping, which, in turn, may produce tissue inclusion. Deep sutures predispose to necrosis of surrounding tissue, epithelial downgrowth, and excessive fibroblastic proliferation.

In only one previous case has the eye been studied four days after cataract extraction, in the case reported by A. Fuchs,[3] in 1935; in his case, however, the

Dr. Edgar B. Burchell prepared the microscopic sections.

From the Eno Laboratory, New York Eye and Ear Infirmary.

Presented at a meeting of the New York Academy of Medicine, Section of Ophthalmology, March 17, 1952.

1. Purtscher, E.: Histologische Frühuntersuchungen nach intracapsulärer Staroperation, Arch. Ophth. **144**:669, 1942; cited by Dunnington, J., and Regan, E.: Effect of Sutures and of Thrombin upon Ocular Wound Healing, Am. J. Ophth. **35**:167, 1952. Maggiore, L.: Ricerche istologische, con deduzioni cliniche, sui processi riparativi normali ed anormali della ferita corneale e sul decorso ed esito delle varie complicanze negli occhi operati di cataratta, Ann. ottal. e clin. ocul. **68**:561, 641, 721, and 881, 1940; **69**:1 and 65, 1941; cited by Dunnington, J., and Regan, E.: Effect of Sutures and of Thrombin upon Ocular Wound Healing, Am. J. Ophth. **35**:167, 1952. Linnen, H. J.: Beobachtungen an der Spaltlampe über den Verschlussmechanismus von Hornhautwunden an Meerschweinchenaugen nach zentraler Trepanation, Klin. Monatsbl. Augenh. **117**:606, 1950. Buschke, W.: Morphologic Changes in Cells of Corneal Epithelium in Wound Healing, Arch. Ophth. **41**:306, 1949.

2. Dunnington, J. H., and Regan, E. F.: Effect of Sutures and of Thrombin upon Ocular Wound Healing, Am. J. Ophth. **35**:167, 1952.

3. Fuchs, A.: Über seltene pathologische Befunde nach Verletzungen, Klin. Monatsbl. Augenh. **95**:721, 1935.

extraction was extracapsular and sutures were not used. Healing was achieved by fibrous tissue proliferation, within the meshes of which were noted the foreign body type of giant cells. The present sections are of paramount interest, since they demonstrate changes which take place in a globe immediately after operation.

HISTOLOGIC REPORT

The eye was submitted for study to the Eno Laboratory of the New York Eye and Ear Infirmary, with the following history: A white man aged 54 consulted his oculist with the complaint of poor vision in the left eye for one year. Examination revealed that the right eye had vision of 20/20 and was normal in all respects. Vision in the left eye was limited to light perception and projection. An almost mature cataract prevented an adequate study of the interior of the globe. Tension was normal. The findings on transillumination were suggestive of a mass on the temporal side, but were by no means conclusive. It was decided to extract the lens, and this was done in the following manner: A Graefe knife incision made superonasally, i. e., opposite the suspected area, was enlarged with Westcott scissors. Three chromic absorbable surgical (catgut) corneoscleral sutures were placed at 9, 11, and 1 o'clock; iridectomy was performed at 11 o'clock, and the lens was delivered in capsule with forceps. Closure was completed by means of a fornix-based conjunctival flap. Funduscopic examination and transillumination immediately after operation, while the patient was still on the table, established the diagnosis of malignant melanoma. The eye was enucleated four days later.

Gross examination of the globe revealed a rather large malignant melanoma of the choroid and ciliary body. The mass had perforated the lamina vitrea and bulged well into the vitreous. The tumor had extended along the suprachoroidal space into the canal of Schlemm on the temporal side. The site of the cataract incision was the limbus on the opposite side.

Figure 1*a* shows the incision under high-power magnification. The lips of the wound are apparently well approximated; however, since the section was taken near the periphery, good apposition of tissues (*A*) would be expected. A moderate amount of round-cell infiltration and a large hemorrhage around the major arterial circle of the iris are seen at *B*. There is blood in the canal of Schlemm (*C*). The inflammatory reaction is a common occurrence when there is manipulation of delicate uveal tissue. In a statistical study, Davis [4] attributed the lower incidence of iridocyclitis with Graefe incisions to minimal trauma and superior wound healing, as compared with the conditions attending keratome-scissors incision.

Farther posteriorly, the incision becomes somewhat curved, probably owing to cutting with scissors at this point (Fig. 1*b*). Descemet's membrane has been peeled off and is incarcerated in the posterior lips of the wound (*A*).

In figure 2*a* is presented the anterior epithelial triangle (*A*), which has evidently plugged the anterior lips of the wound in this region of the incision. However, there is posterior gaping, with resultant iris inclusion (*B*). Descemet's membrane has been stripped from the cornea and bowed backward into the iris. The stripping of the membrane was perhaps a result of manipulation with the spatula or scissors; the elastic lamella undoubtedly accounts for the backward curling.

Figure 2*b* shows an interesting feature, an island of cornea isolated by double cutting (*A*). This may occur oftener than is suspected with the use of scissors. It predisposes to a weak wound and tissue inclusion (*B*).

Figure 3*a* is a section taken at the site of complete iridectomy. The large hemorrhage (*D*) at the major arterial circle is probably traumatic in origin, possibly the result of manipulation of the iris with forceps or scissors, or of trauma in doing the iridectomy through a large vessel. It has been shown [5] that there is great variability in the formation, structure, and loca-

4. Davis, F. A.: Incision and Closure of Wound in Cataract Operations: Study of Graefe Knife Versus Keratome-Scissors Incision and Method of Suture of Deep Wound, Arch. Ophth. **44**:175, 1950.

5. Mann, I.: Developmental Abnormalities of the Eye, London, Cambridge University Press, 1937, Chap. 7.

Fig. 1.—(*a*) Cataract incision (*A*); hemorrhage and inflammatory reaction around major arterial circle of iris (*B*); blood in canal of Schlemm (*C*).

(*b*) Incarceration of Descemet's membrane in posterior lips of wound (*A*).

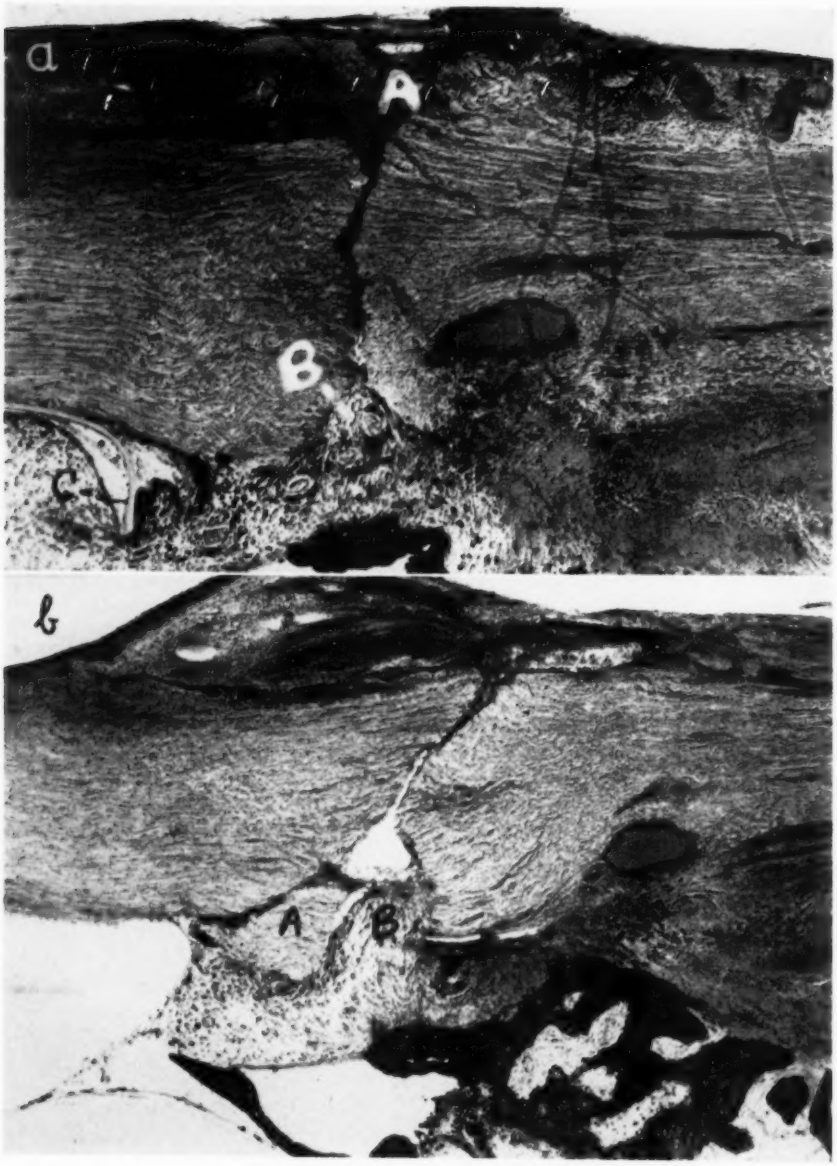

Fig. 2.—(*a*) Anterior epithelial triangle (*A*); iris inclusion in wound (*B*); stripping off of Descemet's membrane and incorporation into iris (*C*).

(*b*) Island of corneal tissue isolated by double cutting (*A*); iris inclusion in area of posterior gaping (*B*).

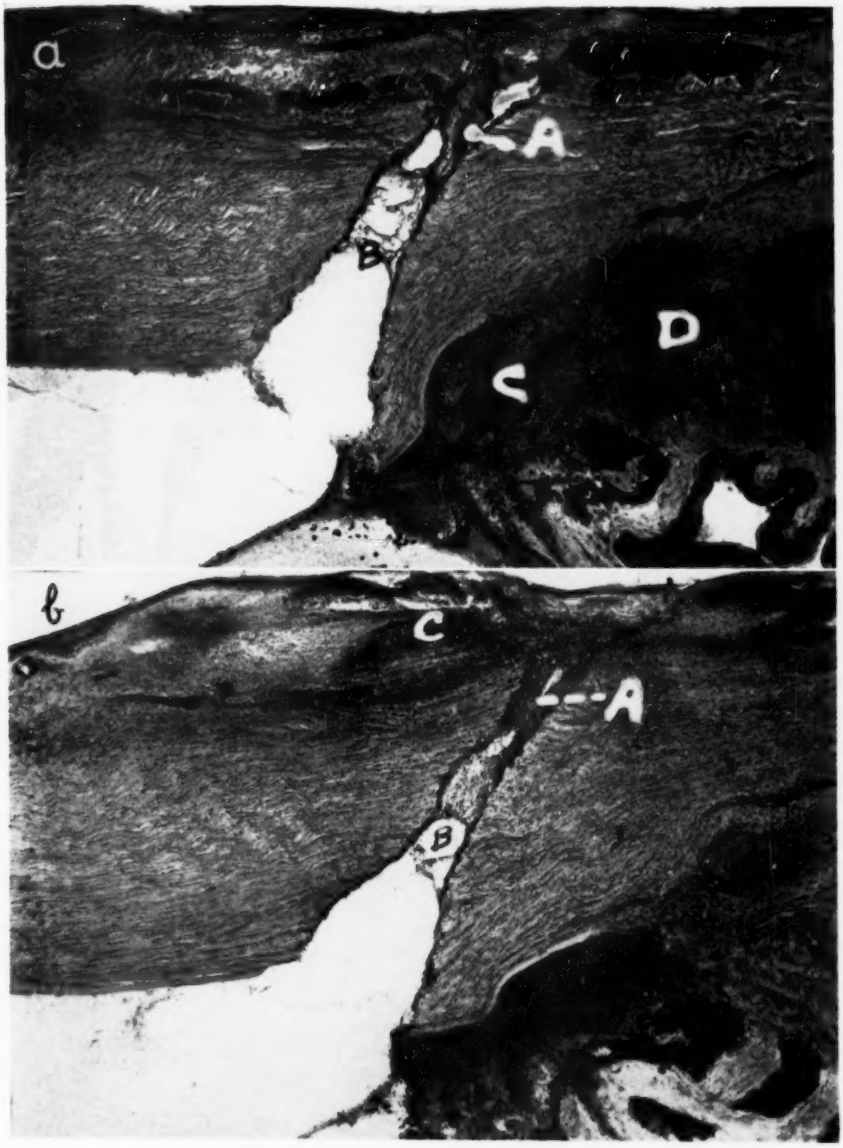

Fig. 3.—(*a*) Fibrovascular plug from surrounding episclera (*A*); posterior gaping (*B*); root of iris (*C*); ciliary hemorrhage (*D*).

(*b*) Fibrovascular closure of anterior half of wound (*A*); posterior gaping (*B*); inflammatory reaction of limbus (*C*).

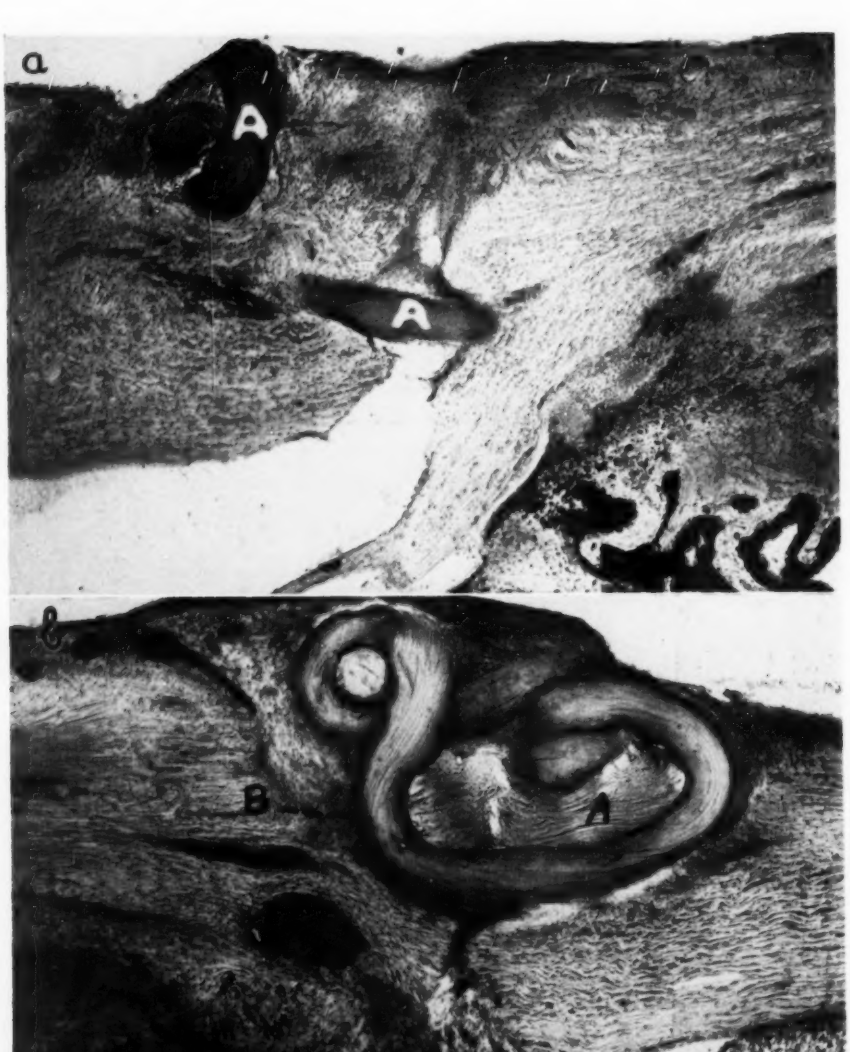

Fig. 4.—(*a*) Reaction around chromic absorbable surgical (catgut) suture (*A*). (*b*) Necrosis of sclera (*A*) in area contained by suture; epithelization (*B*) around suture.

Fig. 5.—(*a*) Epithelization (*A*) around suture; inflammatory reaction in wound (*B*); iris inclusion (*C*); stripping off of pigment epithelium (*D*).

(*b*) Suture (*A*); jagged edges of wound (*B*); iris inclusion (*C*); loss of pigment epithelium of iris (*D*).

tion of the iris vessels. The presence of an abnormal anastomosis may be responsible for a hemorrhage of this type during iridectomy. The fibrovascular plug (*A*) sends delicate extensions into the wound but has not prevented posterior gaping, which is considerable in this zone.

Figure 3*b* demonstrates still deeper extensions from the fibrovascular plug (*A*) in an attempt to offset the marked posterior gaping (*B*). There is a moderate limbal reaction (*C*).

Figure 4*a* demonstrates the inflammatory reaction around the chromic absorbable surgical (gut) sutures (*A*). There are many reports in the literature regarding the advantages and disadvantages of the various types of suture material used in cataract surgery. In an exhaustive study, Hughes and associates [6] came to the conclusion that absorbable suture material produced uniformly more tissue reaction during the first three days after cataract extraction than did nonabsorbable material. The latter produced more irritation after the first week. However, the final gross and microscopic pictures were reported as being the same regardless of the nature of the suture material used. Farris [7] found that chromic absorbable surgical sutures incite less reaction than do plain absorbable surgical sutures.

A section through an entire suture (Fig. 4*b*) shows the area of necrosis (*A*) of the sclera in the region crushed by the suture. As emphasized by Dunnington,[2] tight sutures produce an area of weakening in the wound, with subsequent seepage. Epithelization (*B*) is evident around the suture. Undoubtedly, some degree of epithelization exists when sutures are placed in corneal tissue. With good tissue apposition, the epithelium does not extend into the anterior chamber but merely surrounds the suture material itself. The nature of the suture material does not play the dominant role in epithelial downgrowth; it is the technique in placement which is the determining factor.

Figure 5*A* further demonstrates the epithelization (*A*) around the suture, the inflammatory reaction in the lips of the wound (*B*), and the iris inclusion (*C*). The posterior pigment layer of the iris has been peeled or stripped off (*D*). The last change is probably traumatic in origin.

In Figure 5*B* the edges of the wound are jagged (*B*), but this type of wound healing appears far firmer in this instance, than a so-called clean-cut wound. The suture is seen at *A*, the iris inclusion at *C*, and the loss of pigment epithelium at the iris at *D*.

Generalized conclusions cannot be drawn from one case alone; nevertheless, the findings illustrated in this paper may serve as a guide and clue to the nature of the process in ocular wound healing, in addition to pointing out some early intraocular changes after cataract extraction.

SUMMARY

The findings on histologic examination of an eye four days after cataract extraction were as follows:

1. Wound healing at the limbus began by fibrovascular proliferation and anterior epithelization.

2. Epithelization and inflammatory reaction occurred around chromic absorbable surgical sutures.

3. Despite the use of appositional sutures, there was posterior gaping of the wound, with resultant tissue inclusion.

4. There was evidence of considerable trauma, namely, detachment of Descemet's membrane and hemorrhage around the major arterial circle of the iris.

5. Necrosis of the sclera was produced by the suture.

6. Hughes, W. L.; Guy, L. P., and Romaine, H. H.: Use of Absorbable Sutures in Cataract Surgery, Arch. Ophth. **32**:362, 1944.

7. Farris, J. M.: Tissue Reactions to Suture Materials: A Preliminary Report, Ann. Surg. **114**:159, 1941.

CULTIVATION OF VIRUS OF EPIDEMIC KERATOCONJUNCTIVITIS ON CHORIOALLANTOIC MEMBRANE OF FERTILE EGG

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EPIDEMIC keratoconjunctivitis is a distinct entity which is characterized principally by sudden onset of acute follicular conjunctivitis, glandular adenopathy, and the occurrence of small infiltrates in the deeper epithelium and Bowman's membrane. As the name implies, it occurs in epidemic form, and it was recently prevalent throughout the world.

There was considerable uncertainty as to the exact nature of the etiologic agent of epidemic keratoconjunctivitis. Wright,[1] who in 1930 isolated a filter-passing agent which would produce keratitis in human volunteers, was the first of the advocates of the viral etiology. The identity of a specific virus as the etiologic agent of epidemic keratoconjunctivitis was established in 1943 by Sanders.[2] He was able to isolate the agent from two patients by inoculating mice intracerebrally. The virus became attenuated in serial passage in mice but was increased in potency when it was passed through special tissue culture media for several generations.

Epidemics of keratoconjunctivitis, such as occurred in various parts of the world during World War II, did not appear in Turkey. Only a few sporadic cases were available in the winter of 1951. A study was made of 25 patients with epidemic keratoconjunctivitis, and attempts were made to isolate and to cultivate the virus on the chorioallantoic membrane of developing chick embryos.

Dresel and associates[3] (1941) were the first to report that they took corneal scrapings in clinical cases of epidemic keratoconjunctivitis and transplanted them to the chorioallantoic membrane of the developing chick embryo and obtained death of chick embryos in three to four days. They were able to keep the virus viable through many passages. Calkins and Bond[4] (1944) adapted the original mouse-brain strain of Sanders to the chorioallantoic cavity. Both these investigators failed to demonstrate characteristic lesions on chorioallantoic membrane.

From the Ziya Gün Institute for Research in Trachoma, University of Istanbul.

1. Wright, R. E.: Superficial Punctate Keratitis, Brit. J. Ophth. **14**:257, 1930.

2. Sanders, M., and Alexander, R. C.: Epidemic Keratoconjunctivitis, J. Exper. Med. **77**:71, 1943.

3. Dresel, E. G.; Weineck, E., and Meding, B.: Über die Virusnatur der epidemischen Keratoconjunctivitis, Klin. Wchnschr. **20**:999, 1941.

4. Calkins, H. E., and Bond, G. C.: Adaptation of Virus of Epidemic Keratoconjunctivitis to the Development in Extra-Embryonic Fluids of the Chick Embryo, Proc. Soc. Exper. Biol. & Med. **56**:46, 1944.

In this communication, I shall report the recovery of an infectious agent from four patients with epidemic keratoconjunctivitis. The virus has been maintained by culture on the chorioallantoic membrane of the developing chick embryo and passed indefinitely. The virus can be transmitted to adult mice by the intracerebral route, with results similar to those of Sanders.

CULTIVATION AND PASSAGE OF VIRUS

All material for chorioallantoic culture was obtained from the patients' eyes through conjunctival scrapings, which were collected and diluted with "penicillin-streptomycin" solution. The material was controlled for sterility by culturing aerobically in nutrient broth and on blood agar. The chorioallantoic membrane of fertile chicken eggs was then inoculated with 0.10 cc. of the material.

Conjunctival material taken from the patients in the beginning of this experiment failed to produce lesions on the chorioallantoic membrane, while the mice inoculated intracerebrally with the same material showed the typical picture of roughened fur, hunched back, and lethargy.

Fig. 1.—The eye in epidemic keratoconjunctivitis.

A new attempt to inoculate the material was successful in producing takes on the chorioallantoic membrane onto which human cornea had been transplanted, as described by Kirber and others (1950) [5] and by Sezer (1950).[6]

TECHNIQUE AND MATERIAL

Case 1.—The patient presented in his left eye the characteristic features of epidemic keratoconjunctivitis. The conjunctiva of the lower lid was edematous, and chemosis was intense. Slit-lamp examination of the cornea showed several subepithelial opacities, of varying size. The preauricular node on the side of the affected eye was tender and enlarged (Fig. 1).

April 18, 1951: Two human corneas were divided in seven pieces and transplanted onto the chorioallantoic membranes of 10-day-old developing chick embryos.

5. Kirber, H. P.; Kirber, M. W., and Henle, W.: Transplantation of Cornea to Chorio-Allantoic Membrane, with Observations on Virus Inoculation, Proc. Soc. Exper. Biol. & Med. **73**:481, 1950.

6. Sezer, F. N.: Cultivation of Conjunctival and Corneal Tissue on the Chorio-Allantoic Membrane, Arch. Ophth. **44**:703, 1950.

April 24: The seven corneal transplants were regrafted to seven new chorioallantoic membranes.

The conjunctival scrapings taken from the patient were placed in a "penicillin-streptomycin" mixture, and the seven corneal transplants were inoculated with 0.3 cc. of this material. The infective material was dropped onto the corneas and the surrounding chorioallantoic membrane.

April 28: Neither the cornea nor the chorioallantoic membranes showed any macroscopic lesion.

Chorioallantoic membranes and infected cornea were pooled and emulsified and passed on to five new chorioallantoic membranes.

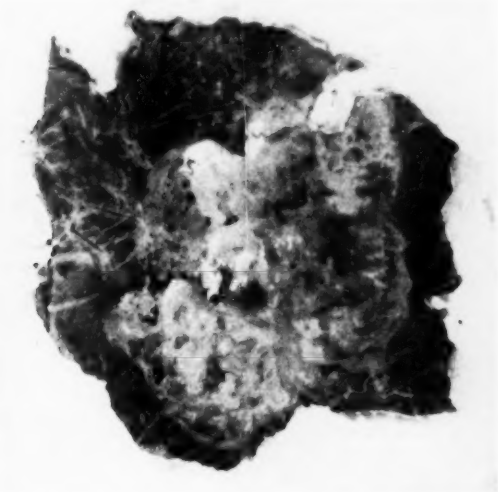

Fig. 2.—Lesion of keratoconjunctivitis virus on chorioallantoic membrane of developing chick embryo.

April 30: Three of the chorioallantoic membranes showed a white area of dense opacity about 1.5 cm. in diameter, with a crater-shaped pock with numerous hemorrhagic spots (Fig. 2). These chorioallantoic membranes were pooled and emulsified (Fig. 3). The emulsion (0.02 cc.) was injected intracerebrally into three mice and also passed on to five new chorioallantoic membranes. Definite signs, such as rough coat, lethargy, and hunched back, appeared in the inoculated mice in 48 hours, and all chorioallantoic membranes showed the same lesions as those described above.

As shown in Figure 3, the virus was found to maintain its potency while being carried through 20 generations of chorioallantoic passage, regularly producing typical lesions on the chorioallantoic membrane and killing the mice in three to five days.

CASE 2.—The virus in Case 2 (Fig. 4) was isolated on the 11th day of the disease by inoculating with the conjunctival scrapings two chorioallantoic membranes of developing chick embryos which were grafted with human cornea. The agent was subsequently carried through 10 generations on chorioallantoic membranes. The virus was transferred to mouse brain and then passed again through eight generations on the chorioallantoic membrane.

CASE 3.—Material taken from the patient (Fig. 5) failed to produce lesions on chorioallantoic membranes which were grafted with human cornea. Three mice were inoculated intracerebrally with the same material. They showed typical symptoms in 48 hours and died on the

fifth day after inoculation. Ground-brain emulsion from the mice produced typical lesions on six chorioallantoic membranes on the second day of inoculation. The virus was passed through eight generations on the chorioallantoic membranes.

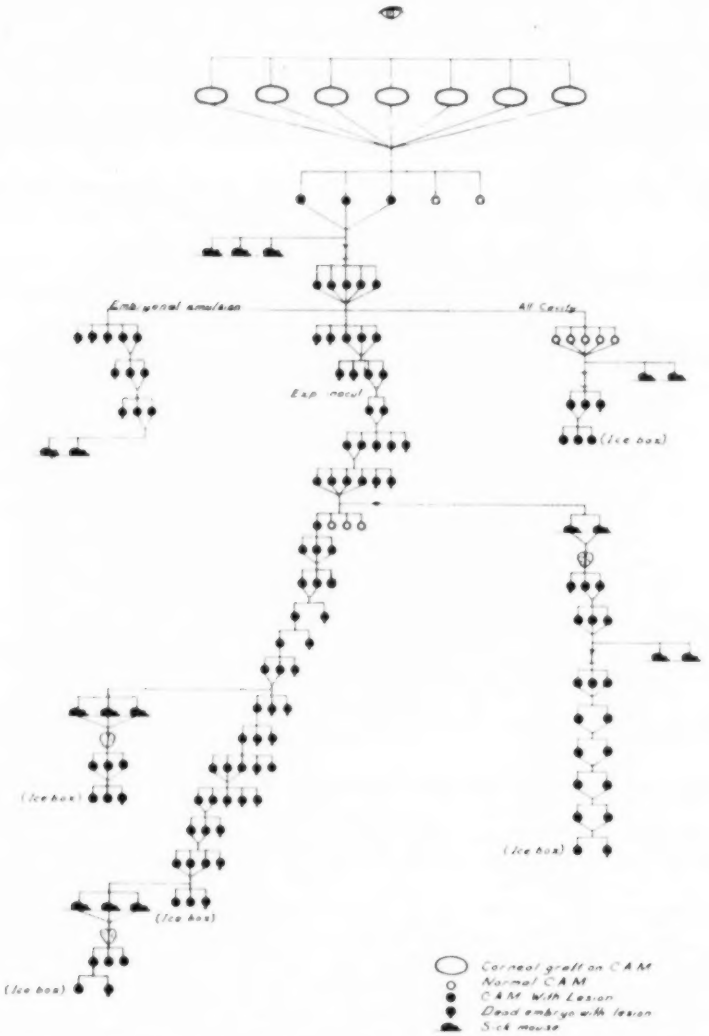

Fig. 3 (Case 1).—Passage of virus through 20 generations on chorioallantoic membranes.

Case 4 (Fig. 5).—The virus was obtained from the conjunctival scrapings, and the chorioallantoic membrane was inoculated without being grafted with human cornea. The agent was passed through four generations of chorioallantoic membrane but failed to produce any lesion in the fifth generation. Three mice inoculated with this material showed mild signs of illness, and one of them died in eight days.

BEHAVIOR OF VIRUS IN LABORATORY ANIMALS

Once the virus had become adapted to the chorioallantoic membrane of the developing chick embryo, its activity in laboratory animals was readily defined.

Pathogenicity for Mice.—In adult mice two days after injection of the virus suspension of chorioallantoic membrane by the intracerebral route lethargy, humped back, ruffled coat, and spastic paralysis developed; the animal died within 24 hours after onset of illness. The infection could be transmitted serially to chorioallantoic membrane from infected brain material.

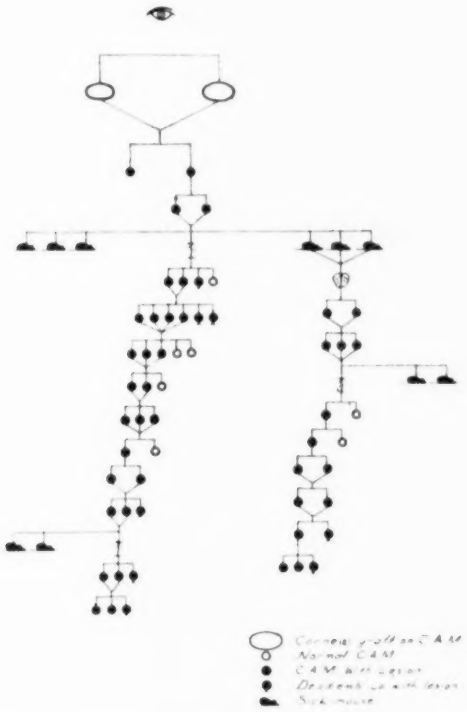

Fig. 4 (Case 2).—Passage of virus through 10 chorioallantoic membranes.

Pathogenicity for the Rabbit.—Inoculations of the rabbit cornea with infected material from human conjunctival scrapings, from chorioallantoic membrane, and from tissue culture consistently failed to produce takes. None of the animals at any time showed lesions on the corneal tissue.

TISSUE CULTURE

Technique.—The clotted plasma method was used. A disc of the superficial layers of the human cornea, removed immediately after enucleation of the eye, was placed on a cover slip, covered with a drop of nutrient fluid, and then picked up with a slide coated with petrolatum (vaseline®). The nutrient fluid consisted of rabbit plasma, 2 parts; rabbit serum, 2 parts, and

chick embryo extract, 1 part. The cultures were incubated at 37 C. Four days after incubation the tissue culture was inoculated with 3 drops of a suspension of the infective agent and left in the incubator for three days at 37 C. For the purpose of passage, inoculated tissue was ground up and used in inoculation of four chorioallantoic membranes of fertile eggs and in intracerebral injection of two mice.

The eggs showed lesions, and the mice became ill, in 48 hours.

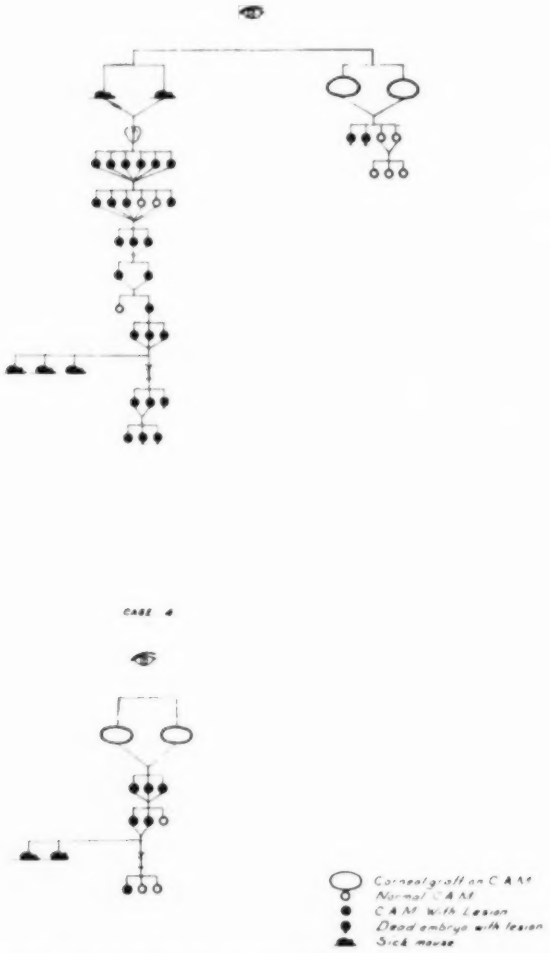

Fig. 5 (Cases 3 and 4).—*A* (Case 3), passage of virus through eight generations on chorioallantoic membranes; *B* (Case 4), passage of virus through four generations on chorioallantoic membranes.

EXPERIMENTAL EPIDEMIC KERATOCONJUNCTIVITIS IN HUMAN VOLUNTEERS

For further evidence of a specific relation of the isolated virus to human disease, the virus from chorioallantoic membranes on the sixth passage in Case 1 and from membranes on the third passage in Case 3 were transferred to the eyes of two

volunteers. A mild, but characteristic, disease appeared on the third day—slight conjunctivitis, with several follicles and subepithelial infiltrations in the cornea. Edema or enlargement of preauricular glands was not observed. The follicles disappeared in the first week, but infiltration of the cornea persisted for two months.

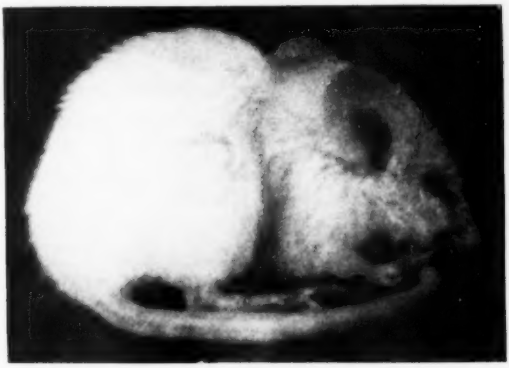

Fig. 6.—Mouse three days after intracerebral injection with chorioallantoic-membrane strain of virus of keratoconjunctivitis.

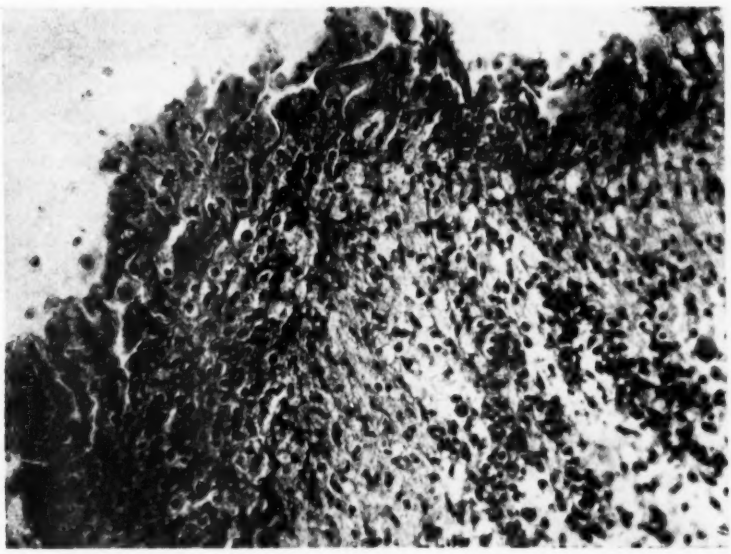

Fig. 7.—Section from lesion of chorioallantoic membrane infected with virus of keratoconjunctivitis. Note proliferation of ectodermal cells, associated with necrosis and vacuolation.

MICROSCOPIC APPEARANCE OF MEMBRANE LESIONS

Membrane lesions were removed for histologic study from living embryos on the third day after inoculation. Microscopically, the lesions exhibited a morpho-

logic feature characteristic of virus infection, namely, hyperplasia and hypertrophy of ectodermal cells, associated with varying degrees of necrosis and vacuolation.

PROPERTIES OF THE VIRUS

Filtration.—A 10% suspension in sterile Tyrode solution of virus material pooled from the 14th generation in Case 1, from the 8th generation in Case 2, from the 6th generation in Case 3, and from the 2d generation in Case 4 was stored in the ice box. The fluid was passed through a Seitz E. K. filter which contained a double pad. The filtrate produced typical symptoms in five mice on intracerebral inoculation and typical lesions on three of five chorioallantoic membranes in 48 hours.

TABLE 1.—*Filtration of Chorioallantoic Membrane Virus Through E. K. Seitz Filter (Double Pad)**

Material Tested	No. of Days After Inoculation	Inoculation of †	
		Chorioallantoic Membrane	Mouse Brain
Infected chorioallantoic membrane mixture before filtration	1	— — — — —	— — — — —
	2	+ + + — —	+ + — — —
	3	D D + + +	D + + + +
		D D +	D + + +
		D	D D D
Filtrate of infected chorioallantoic membrane mixture	1	— — — — —	— — — — —
	2	+ + — — —	+ + + — —
	3	+ + + — —	+ + + — —
	4	D D + — —	D D D — —
	5	D — —	— —

* Tested by inoculation of chorioallantoic membrane and intracerebral injection into mice.
† D indicates dead embryo or mouse; plus signs (+), sick animal or lesions in membrane.

TABLE 2.—*Neutralization of Chorioallantoic-Membrane Virus by Convalescent and Normal Serums*

Serum	No. of Days After Inoculation	Virus Dilutions Used in Inoculation of Eggs *				
		1:10	1:100	1:1,000	1:10,000	1:100,000
Normal	1	— — +	— — —	— — —	— — —	— — —
	2	+ + +	+ + +	— + +	— + +	+ + +
	3	D D +	D + +	+ + +	+ + +	+ + +
	4	D	D +	D + +	D + +	+ + +
Convalescent serum (Case 2)	1	— — +	— — —	— — —	— — —	— — —
	2	+ + +	D + +	— — +	— — —	— — —
	3	D D +	+ — +	— + D	— — —	— — —
	4	D	D D	+ +	— — —	— — —

* Indicates dead embryo; the plus sign (+), lesions on the chorioallantoic membrane.

No attempt was made to determine the exact size of the virus by ultrafiltration.

Neutralization Test.—The virus material for the neutralization test was obtained from the stock chorioallantoic-membrane virus suspension which was used for filtration experiments. Ten cubic centimeters of inactivated and undiluted rabbit serum was added for each gram of membrane tissue. After centrifugation at about 2,000 rpm for 10 minutes, the supernatant fluid was drawn off and regarded as a 1:10 dilution of virus. Starting with this 1:10 dilution, I prepared 1:100; 1:1,000; 1:10,000, and 1:100,000 dilutions, using 10% rabbit serum in saline solution as the diluent.

The neutralization tests were made with (1) convalescent serums from Patients 1 and 3 and with (2) normal human serum. One-half cubic centimeter of virus dilutions ranging from 10^{-1} to 10^{-5} was mixed with the inactivated and undiluted serum to be tested. The material was incubated for one hour at 37 C. and then placed in the ice box at 4 C. for four hours. The chorioallantoic membranes of five eggs were inoculated with 0.25 cc. of each dilution, and 0.03 cc. of each dilution was injected intracerebrally into each of five mice. All mice inoculated with the virus plus the convalescent serum in dilutions from 10^{-3} to 10^{-5} survived, while the control mice (receiving virus plus normal serum) died on injection of dilutions up to 10^{-5}.

COMMENT

The conjunctival material taken from patients in the beginning of these experiments failed to produce a lesion on the chorioallantoic membrane of fertile eggs. The membrane was then grafted with human corneal tissue in order that a suitable medium for the growth of the virus might be obtained. Only after this transplantation did the virus adapt to chorioallantoic membrane. Once the virus was adapted to the membrane, it could be passed successfully, with the same characteristic lesions on the membrane and the inevitable death of the embryo.

After inoculation of the adapted virus, the lesions were found on the chorioallantoic membrane within 48 to 72 hours. The ectodermal cells proliferated, without showing any inclusion bodies. Petechial hemorrhages and thromboses in small vessels were observed. After adaptation to the chorioallantoic membrane, the infection became generalized and brought about the death of the embryo in 24 to 72 hours.

The virus proliferated readily in the allantoic membrane and was found in the allantoic cavity. The presence of infectivity was most easily judged by mouse inoculation or by inoculation of chorioallantoic membranes.

The virus could be kept alive and be passed to chorioallantoic membrane easily in tissue culture.

The neutralization experiments indicated the presence of immune bodies in convalescent serum, as previously shown by Sanders.

The filtration of virus with the E. K. Seitz filter with double pads, the failure to produce any specific lesion on the inoculated rabbit cornea, and the absence of inclusion bodies indicate that the virus differs from the virus of herpes simplex.

SUMMARY AND CONCLUSIONS

A virus was isolated on the chorioallantoic membrane of the developing chick embryo by inoculation with conjunctival scrapings from four patients suffering from epidemic keratoconjunctivitis.

In two cases the primary isolation was made on chorioallantoic membrane grafted with human corneal tissue. In one case conjunctival scrapings were passed to the chorioallantoic membrane without an initial corneal graft, but this material failed to maintain its virulence for more than four generations. In one case the primary isolation of the virus was made by intracerebral inoculation of mice, and the virus was subsequently passed onto the chorioallantoic membrane.

The virus could be kept alive in tissue culture of human cornea.

The chorioallantoic-membrane virus could be neutralized by convalescent serums of two patients from whom the virus had originally been isolated.

After several passages on the chorioallantoic membrane, the virus produced a mild, but characteristic, picture of epidemic keratoconjunctivitis in two human volunteers.

The virus failed to produce pathologic changes on the cornea of the rabbit.

The virus could be filtered through an E. K. Seitz filter with double pads.

The virus isolated on the chorioallantoic membrane was pathogenic for mice by the intracerebral route and produced symptoms similar to those described by Sanders.

The numerous points of similarity strongly suggest that the virus which I have adapted to the chorioallantoic membrane is the same as the virus of epidemic keratoconjunctivitis isolated by Sanders in mouse brain.

INTRAVENOUS USE OF CORTICOTROPIN IN OPTIC NEURITIS

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NEW YORK

THE INTRAVENOUS use of corticotropin (ACTH) in the treatment of optic neuritis merits serious consideration. It is my purpose in this paper to review the current literature on the subject and to illustrate the use of the drug by reporting my experience in the successful treatment of a patient with intravenous administration of corticotropin. The case presented itself shortly after publication of the recent article by Gordon and associates[1] on their experiences with corticotropin and cortisone therapy in acute ocular conditions, in which they stated that "intravenous drip ACTH is the most effective weapon available today," and after Dr. Allan Wood's report at a meeting of the New York Academy of Medicine, Section of Ophthalmology, on the effectiveness of the intravenous use of corticotropin. Current literature on the use of corticotropin in all fields of medicine is voluminous, but relatively few articles are concerned with its intravenous use.[2] In an extensive search of the literature, I discovered no major article reporting its use in ophthalmology. The main points covered in these articles follow.

INTRAVENOUS USE OF CORTICOTROPIN

In 1949 Sayers and associates[3] first demonstrated that corticotropin could be given intravenously in large doses and, further, that it disappeared rapidly from the blood stream in normal subjects, while giving rise to a maximum, but transient, stimulation of the adrenal cortex. Doses of 50 and 100 mg of corticotropin in 200 cc. of saline were given over periods varying from one-half to one hour. Gordon[2b] then pointed out that the administration of corticotropin in continuous intravenous drip for approximately eight hours or more led to sustained adrenocortical stimulation in human subjects, and he emphasized that relatively small quantities were required. The underlying physiological mechanism seems to be that the pituitary adrenocorticotropic hormone is normally discharged continuously

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1. Gordon, D. M., and others: Use of ACTH and Cortisone in Ophthalmology, Am. J. Ophth. **34**:1675-1686 (Dec.) 1951.

2. (*a*) Gordon, D. M., and others.[1] (*b*) Gordon, E., in Proceedings of the Second Clinical ACTH Conference, edited by J. R. Mote, Philadelphia, The Blakiston Company, 1951. (*c*) McIntosh, H. W., and Holmes, C. B.: Intravenous Use of ACTH, Canad. M. A. J. **65**:33-35 (July) 1951. (*d*) Mandel, W., and others: Intravenous Use of Pituitary Adrenocorticotropic Hormone (ACTH): A Report on Its Administration in 25 Patients, J. A. M. A. **146**:546-551 (June 9) 1951. (*e*) Renold, A. E., and others: Intravenously Administered ACTH: A Preliminary Report, New England J. Med. **244**:796-798 (May 24) 1951.

3. Sayers, G., and others: Metabolic Actions and Fate of Intravenously Administered Adrenocorticotropic Hormone in Man, J. Clin. Endocrinol. **9**:593-641 (July) 1949.

into the blood stream in fluctuating amounts, as required by the environmental conditions; that is, a tonic activity, or base line secretion, exists, and that when the "alarm reaction" is called into play the pituitary-adrenal system is "stepped up" as part of the response complex needed to meet successfully the stress situation. That maximal secretory activity in a target gland may be expected when the stimulation is constant, rather than intermittent, is a basic principle of endocrine physiology. Gordon [2b] and Ingle [4] have shown this axiom to hold in the case of corticotropin stimulation of the adrenal cortex.

Clinical experimentation on normal volunteers by McIntosh and Holmes,[2c] using intravenous [5] doses ranging from 2.5 to 160 mg. of corticotropin, has shown that the degree of adrenocortical stimulation attained by the continuous intravenous administration is considerably greater than that achieved by the use of the intramuscular route. Their figures show, furthermore, that a maximum degree of adrenocortical stimulation occurs with a relatively small dose of corticotropin (approximately 10 mg.) when given by continuous intravenous infusion over a 24-hour period. The degree of adrenocortical stimulation measured over a 24-hour period is proportional to the length of time over which the corticotropin is given, being maximal, in fact, when the corticotropin is administered over the whole 24-hour period. These authors recommend that a dose of 10 to 20 mg. of corticotropin be given intravenously over the full 24 hours. Other authors are of the opinion that the administration of 5 to 20 mg. over a period of 8 to 12 hours is suitable in most cases, and that it is more practical in application than the longer courses.

Preliminary clinical reports, covering large series of patients and a wide variety of diseases, are now available. Renold and associates [2e] reported on a series of 100 cases, while Mandel and co-workers [2d] reported 25 cases and later added 80 to their series. These reports confirm the points presented above and present several others, which are briefly summarized as follows:

1. Corticotropin can best be administered in 500 to 2,000 cc. of either 5% dextrose in distilled water or isotonic sodium chloride solution, which is run in over a period of 8 to 24 hours. Salt restriction and the addition of 0.2% potassium chloride to the solution is advisable. The blood pressure, weight, results of urinalysis, and eosinophile counts should be recorded at intervals (not necessarily daily).

2. If the patient is placed in a wheel chair and a vein in the forearm is used, he can usually be made semiambulatory.

3. Qualitative control of the adrenocortical activation may be obtained by measuring the fall in circulating eosinophiles, which in normal subjects under intravenous therapy is 60% in four hours and 96% in eight hours. Eosinophile counts of less than 11 per cubic millimeter are common (i. e., none are seen). In experimental work, quantitative control can be obtained, if desired, by measuring the rise in the 24-hour urinary 17-ketosteroids—an increase of 10.8 mg. being observed normally. While this method is a reliable test of the adrenal cortex reserve, its use is entirely unnecessary in clinical practice.

4. Ingle, D. J.: Biologic Properties of Cortisone-Review, J. Clin. Endocrinol. **10**:1312-1354 (Oct.) 1950.

5. The term "intravenous" in this paper refers to continuous drip administration over approximately eight hours or more.

4. Continuous intravenous administration of corticotropin results in an enormous increase in secretory activity of the adrenocortex, as compared with the intermittent stimulation which results from the usual method, of intramuscular injection.[2c, e] Gordon [2b] showed a twentyfold increase in response to corticotropin given intravenously over a 12-hour period over the response to the same dose given by a single intramuscular injection. Renold and associates [2e] stated that at the end of 24 hours 20 mg. given intravenously over an eight-hour period results in 5 to 10 times the effect that 20 mg. of corticotropin given intramuscularly every six hours (total dose, 80 mg.) does. Finally, Mandel and co-workers [2d] claimed that 2.5 mg. of corticotropin given intravenously over 24 hours has the same result as 20 mg. given intramuscularly every six hours (80 mg. a day). These various figures are in approximate agreement and serve to emphasize the potency of the intravenous route. It is also to be noted that intermittent intravenous administration appears to be more effective than intermittent intramuscular injections and that continuous intravenous drip is more effective than continuous intramuscular administration.

5. When 20 mg. of corticotropin is given intravenously daily to a normal patient, a maximum response is attained in from three to eight days, after which the degree of activation remains about the same with repeated infusions at the same dose level.

6. Response versus dose is linear in the range of 1 to 15 mg. and then levels off, so that the response to 40 mg. is the same as that to 20 mg. (both maximal) in normal patients.

7. Intravenous administration of corticotropin may result in a normal adrenal response in patients who have become unresponsive to the same preparation by the intramuscular route.

8. It appears that a tissue factor is responsible for the destruction of some of the physiological activity of corticotropin when it is given intramuscularly. Inactivation of the hormone by muscle enzymes has been demonstrated by Dr. C. H. Li.[2d]

9. Subjective improvement is obtained earlier by giving the corticotropin intravenously, and usually is noted on the second and third days. The clinical improvement is more complete and the remission generally more prolonged than occurs after much larger doses given intramuscularly.

10. Many patients can be maintained on daily doses of less than 5 mg. (2.5 to 5 mg). Patients who require higher daily maintenance doses often relapse promptly when the medication is discontinued.

11. In spite of the reported diurnal variations [6] in adrenocortical activity, there does not appear to be any marked difference in effect when the infusions are given during the day or when given during the night.

12. Most patients show a distinct increase in appetite during treatment, but the weight gained is usually lost subsequently.

13. The change in the eosinophile count and in the sedimentation rate occurs earlier and is more pronounced in the patients treated with intravenous injections of corticotropin than in those treated by the intramuscular route.

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6. Best, W. R., and Santer, M.: Variation and Error in Eosinophile Counts of Blood and Bone Marrow, Blood **6**:61-74 (Jan.) 1951. Elmadjian, F., and Pincus, G.: A Study of the Diurnal Variations in Circulating Lymphocytes in Normal and Psychotic Subjects, J. Clin. Endocrinol. **6**:287-294 (April) 1946.

14. No significant alteration occurs in the red blood cell count, hemoglobin, or serum proteins, but a polymorphonuclear leucocytosis usually is observed.

15. Common complaints during the first few hours of infusion are flushing of the face, a feeling of tightness across the chest, and a sense of fullness in the abdomen. The slower the rate of infusion, the less frequent these complaints become. Signs and symptoms suggestive of Cushing's syndrome, such as acne, moon-shaped face, fluid retention, and hypertension, are seen in some of the cases,[2d] but they tend to disappear with reduction of the dose or interruption of administration. Varying degrees of euphoria may occur, but psychoses have not resulted in these series. According to Renold [2e] no anaphylactic phenomena have yet been reported, although repeated intravenous infusions have been given to patients over periods as long as 16 weeks. Some cases of sensitivity to intramuscular administration of corticotropin have been reported. It thus seems that untoward reactions may, perhaps, be slightly more frequent and may occur with greater rapidity with intravenous than with intramuscular use, and therefore patients receiving intravenous medication should be watched carefully during the first 30 minutes for the appearance of any undesirable effects. However, if such do occur, and the drip administration is continued, the antiallergic effect of the corticotropin comes into play and overcomes the sensitivity.[7]

16. Intravenous administration of corticotropin is cheaper than the intramuscular method, and if more corticotropin is needed one can increase the length of the drip infusion rather than the dose.

In summary, I may say that, although the hormone has been used clinically for several years, relatively little mention has been made of the possibilities of its intravenous use (June, 1951). Some of the reasons [2d] for this are (*a*) the impurities in the substance, which act as foreign protein, and thus are a potential hazard; (*b*) the belief that intravenous administration would offer no advantages over the more convenient, intramuscular route, and (*c*) the fact that literature supplied by the manufacturer cautions against its intravenous use. The chief reason for this lack of concern is that no one has written a separate paper pointing out the safety of the method, and that most data on the subject lie buried in larger papers. Now, however, the effectiveness of the intravenous drip method of corticotropin medication in man has been fully confirmed, and its use, provided the patient is kept under observation during the early part of the infusion, may be considered safe. The greater effectiveness of intravenous infusion is due to the more continuous adrenocortical stimulation and to the fact that destruction does not occur at the injection site. Only minute amounts of the drug are required, at any given moment, to stimulate the adrenal cortex. It is, perhaps, more effective to prolong the infusion time than to increase the dose beyond 20 mg. The obvious advantages of the intravenous route are that (*a*) it is more economical, (*b*) the therapeutic results are often more satisfactory, (*c*) the problem of refractoriness does not seem to occur, and (*d*) it rapidly reactivates an adrenal cortex suppressed by cortisone therapy. All this means that the intravenous administration of corticotropin is now the most efficient and economical method of stimulating the adrenal cortex. It should be noted, however, that the value of the long-acting acthar® (corticotropin) gel is

7. Harvey, A. McG.: Third Clinical ACTH Conference, April 25 to 26, 1952.

still under investigation. The new high-potency acthar® gel is satisfactory intravenously [8] and is also best given in 1,000 cc. of solution at a rate of 25 to 30 drops per minute.

OPTIC NEURITIS

The subject of optic neuritis has been very well covered on many occasions.[9] Carroll [10] reviewed 240 cases and in his conclusions mentioned that the use of corticotropin and cortisone in optic neuritis was under investigation. Almost concurrently several other authors [11] reported on the intramuscular use of corticotropin in the treatment of this condition, their results ranging from "questionable and nondramatic" to "highly favorable and dramatic." All agreed that much more work is needed to clarify the action of these powerful hormones in the treatment of optic neuritis. Gordon and others [1] reported the use of corticotropin in eight cases of optic neuritis, with but one failure. Both the intravenous and the intramuscular route were used. Since the appearance of this paper, the Cornell group has administered corticotropin intravenously in several more cases,[12] but their results are not as yet reported (June, 1952). They have used doses of from 20 to 80 mg. in 1,000 cc. of dextrose in water over periods of six to eight hours. My own experience with the intravenous use of corticotropin in optic neuritis is limited to two cases. In one of these the condition was diagnosed as "diabetic optic neuritis, right eye," and was in no way improved. The other case will be presented in some detail, to illustrate the excellent results which may sometimes be obtained with the intravenous use of corticotropin.

Mrs. C. R., a 50-year-old woman, spoke only Spanish. In spite of the language difficulty, the following history was obtained: A few days before Christmas she experienced a sudden severe pain in her right eye. A physician was called, and she was given an injection (morphine?) for the pain and advised to see an eye doctor. She felt weak and nauseated, and three days later the vision in this eye became much worse. She did not bother to see an oculist, hoping that she would get better in time by herself. On Jan. 1, two weeks after the onset of pain in the right eye, the pain started in the left eye, and she again felt weak and nauseated and lost vision in the following day or two. On Jan. 8 she came to the clinic of the Manhattan Eye, Ear, and Throat Hospital, for the first time and was admitted to the hospital.

In her past history, the only possible clues that might have a bearing on the condition were (*a*) that in 1943 she had been treated by a physician for sinus trouble and (*b*) that she had had a severe cold for a week, two or three weeks before Christmas, with chills, severe headache (frontal and generalized), pain in and around the right eye and in the back of the neck, and a stuffed-up nose, for which her doctor had given her nose drops.

On admission, the corneas were found to be clear; the conjunctivas were not injected; the scleras were white; the pupil of the right eye reacted poorly to light directly, but in a normal

8. Gordon, D.: Personal communication to the author.

9. Duke-Elder, W. S.: Text-Book of Ophthalmology, Vol. 3, St. Louis, C. V. Mosby Company, 1940, pp. 2967-3058.

10. Carroll, F. D.: Optic Neuritis: A 15-Year Study, Am. J. Ophth. **35**:75-82 (Jan.) 1952.

11. Hogan, M. J., and others: Effect of ACTH and Cortisone on Ocular Disease, Am. J. Ophth. **34**:73-86 (May, Pt. 2) 1951. Olson, J. A., and others: Use of Adrenocorticotropic Hormone and Cortisone in Ocular Disease, A. M. A. Arch. Ophth. **45**:274-300 (March) 1951. Scheie, H. G., and others: Adrenocorticotropic Hormone (ACTH) and Cortisone in Ophthalmology, ibid. **45**:301-316 (March) 1951. Fitzgerald, J. R., and others: Early Clinical Results of ACTH and Cortisone Treatment of Ocular Diseases, ibid. **45**:320-333 (March) 1951. Woods, A. C.: The Present Status of ACTH and Cortisone in Clinical Ophthalmology, Am. J. Ophth. **34**:945-960 (July) 1951.

12. Personal communication to the author from Cornell residents.

way, consensually; the pupil of the left eye reacted normally to light both directly and consensually; tension was normal to finger palpation; the media was fairly clear; the disks were elevated 2 to 3 D; the edge of each disk was hazy and the surrounding retina edematous; the veins were markedly engorged and tortuous, and many small hemorrhages, both punctate and fan-shaped, were seen on and around the disks and in the vicinity of the macular areas. The maculas themselves were, perhaps, a little edematous but otherwise appeared fairly normal; vision in the right eye was limited to light perception with poor projection, but the latter finding

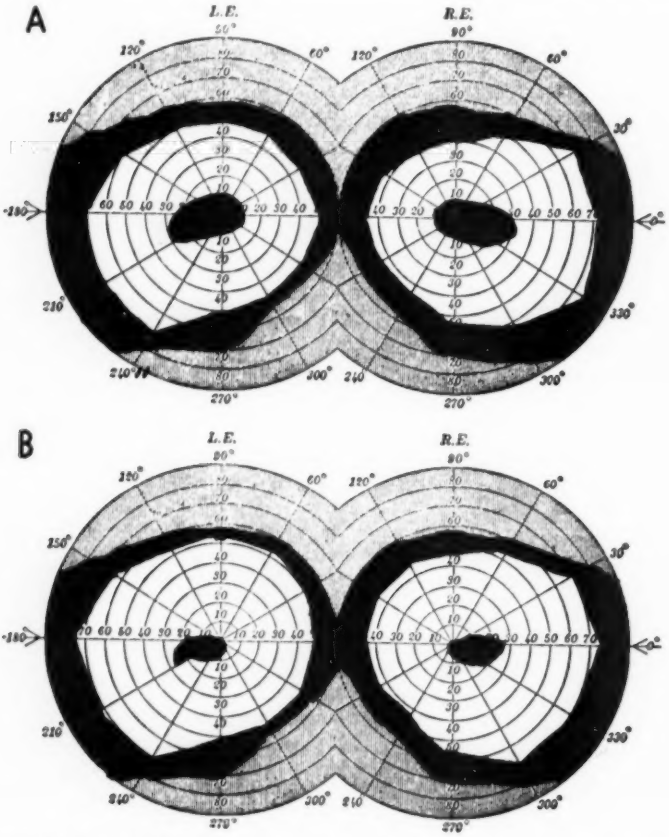

Fig. 1.—*A* (Jan. 9) peripheral visual fields for 5/330 white in the left eye and for 5/330 white in the right eye; vision 1/200 in each eye. *B* (Jan. 19), peripheral fields for 5/330 white; vision 1/200 in the left eye and 10/200— in right eye. There was little change at the peripheral but some reduction of the central scotomas.

may have been due to the language difficulties; vision in the left eye was limited to perception of hand movements only.

The usual history taking and physical examination were completely noncontributory. As complete a laboratory survey as possible was undertaken. Roentgenograms of the sinuses, teeth, chest, optic foramina, and long bones were taken. No abnormalities were noted. An ear, nose, and throat consultant reported chronic tonsillitis but was undecided as to whether chronic sinusitis existed or not (the ethmoid cells were perhaps slightly cloudy). Blood studies revealed a negative Wassermann reaction, normal blood sugar, an elevated sedimentation rate (18 mm. in one hour; normal, 10 mm.), normal serum proteins (6 to 8 gm. per 100 cc.), and an albumin-

globulin ratio of 4.6:2.6, or 1.6. Mantoux tests gave negative reactions to tuberculin in 1:100,000 and 1:10,000 dilutions but a positive reaction in a 1:1,000 dilution. Spinal fluid findings, including the Wassermann reaction, were normal except for pressures of 260 and 180 mm. Since the patient was somewhat lethargic, the idea was briefly entertained that the condition might be a papilledema rather than papillitis. The fundus picture was more that of papillitis, however, and, as the neurological findings and cerebrospinal fluid proteins were normal, the neurological consultant did not consider the cerebrospinal fluid pressures to be significant. Probably the high values found could be explained by the patient's struggling during the

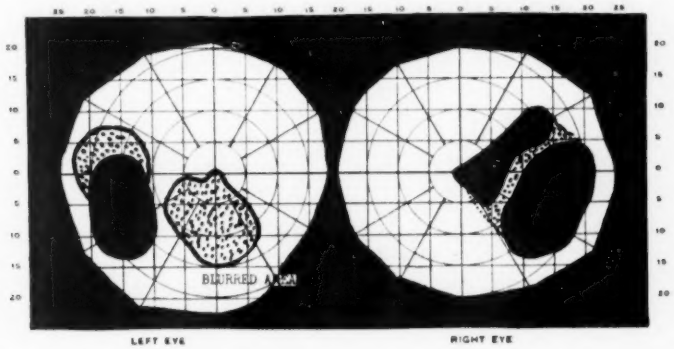

Fig. 2.—Central visual fields for 5/1000 white on Jan. 19. There was questionable fixation in the left eye.

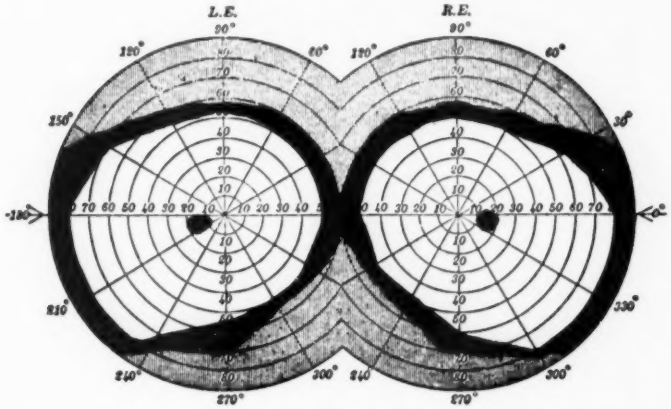

Fig. 3.—Peripheral visual fields for 3/330 white on Feb. 1, with marked improvement. Vision 20/70 in the left eye and 20/50 in the right eye.

procedure. The Widal test (febrile antigen agglutination) gave a positive reaction to antigen O in a titer of 1:40; negative reactions to antigen H and paratyphoid A, a positive reaction to paratyphoid B in a titer of 1:40, and a negative reaction to Proteus OX19. The serum agglutination tests for brucellosis were negative in a titer of 1:20. Thus, as no definite etiologic agent could be found, it was believed that the condition might well be an acute inflammation, secondary to the known preceding infection of the upper respiratory tract, which was assumed, from the history, to be viral.

Treatment was commenced on Jan. 9, with the vision in each eye measuring slightly less than 1/200. Cortisone was ordered to be given orally daily in divided doses, as follows: 300,

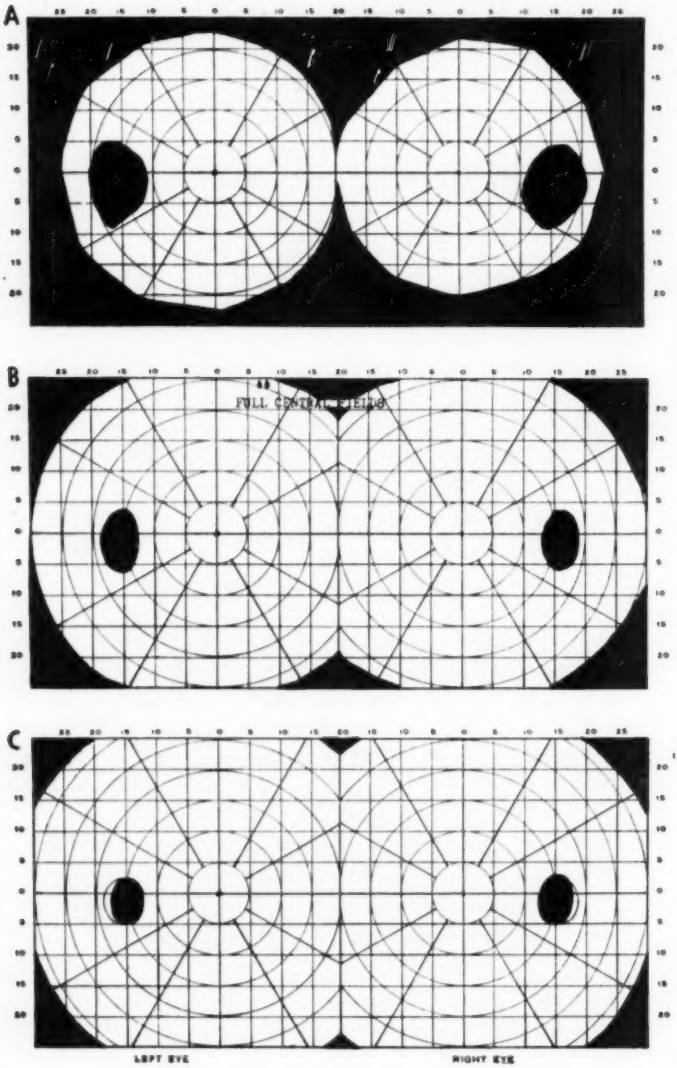

Fig. 4.—Central visual fields for 2/1000 white. *A* (Feb. 1), good fixation; vision, with glasses, 20/40—2 in the left eye and 20/40+2 in the right eye. *B* (Feb. 8), vision, with glasses, 20/30 in the left eye and 20/30—2 in the right eye. *C* (Feb. 22), central fields full with glasses; vision, 20/30 in each eye.

200, and 100 mg., and then 100 mg. thereafter. Three milligrams of chloramphenicol (chloromycetin®) was given immediately, followed by 500 mg. every four hours. Instillations of homatropine and 10% phenylephrine (neo-synephrine®) hydrochloride were ordered three times a day for each eye to dilate the pupils. The following day the patient reported some subjective improvement, but no clinical change had occurred in the vision or the fundus picture. Administration of nicotinic acid was started on Jan. 13, in a dose of 100 mg. three times a day one-half hour after meals. This dosage was increased until 300 mg., given three times a day on the 16th day, caused a pronounced flush and palpitation. The dose was reduced to 100 mg. three times a day, and this amount was well tolerated. There was no change in the fundus on Jan. 15, and at this time a photograph of the fundus was taken. By Jan. 17 vision had improved to 10/200 in the right eye and 1/200 in the left eye. There was no further change in vision or in the fundus picture up to Jan. 22, when treatment with cortisone (total, 1,600 mg.), chloramphenicol, and nicotinic acid was stopped. It was decided to continue the treatment, with corticotropin, although no great hope was held for further gain in vision, as the condition was then of five weeks' duration.

Corticotropin was given during the next 10 days in doses varying from 10 to 40 mg. in 1,000 cc. of 5% dextrose in water. The time over which the intravenous drip was given each day was approximately eight hours, a rate of 30 drops in one minute. Salt was restricted, and potassium chloride was given orally (1 gm. three times a day). Eosinophile counts were taken near the end of the intravenous infusion; daily weights, blood pressures, and urinary findings were recorded. These data are presented in the accompanying Table.

*Data on Administration of Corticotropin in a Case of Optic Neuritis**

Date	Weight, Lb.	Eosinophile Count	Corticotropin, Mg.	Vision Without Glasses		Comment
				O. D.	O. S.	
Jan. 22	160	177	25	10/200	1/200	No change
23	160	166	25	.....	.....	Dizziness
24	161	222-210	20	20/200	10/200	Subjective improvement
25	160	155	35	.....	.....	.....
26	161	299	35	.....	.....	.....
27	161	320	35	20/200	20/100	Eosinophile count not falling
28	161	66-33	40	.....	.....	Response
29	165	11	30	20/70	20/70 + 2	Fundi much improved
30	163	11	20	.....	.....	.....
31	164	22	10	20/50	20/70 + 2	.....
Feb. 1	...	22	Treatment tapered off with cortisone	20/40	20/40 c. glasses	Patient discharged

* The blood pressure remained at 150/100 throughout treatment. The urine was constantly normal. During administration of the 40-mg. dose, on Jan. 28, the patient was very flushed during the latter part of the infusion.

The dose was reduced after the second day, as the patient had complained of feeling dizzy. It is to be noted that subjective improvement was first reported on the third day. The eosinophile count rose slightly, and it was thought advisable to increase the dose of corticotropin, as previous reports [13] had indicated that no improvement would result until a satisfactory fall in eosinophiles was obtained. This point was reached on the seventh day, when the eosinophiles fell from 320 to 33 per cubic millimeter. On the eighth day a notable improvement in visual acuity was recorded, vision being now 20/70 in each eye. The appearance of the fundi had improved over the preceding two or three days, so that less than 1 D. of elevation remained, and the number of hemorrhages had decreased. Marked resolution of the central scotomata had occurred. It was decided to continue the tapering off of cortisone therapy, starting with a dose of 25 mg. (given orally) four times a day and gradually reducing the dose over a week or two.

13. Frazier, C. N.; Lever, W. F., and Keuper, C. S.: Response of Patients with Malignant and Benign Pemphigus to Adrenocorticotropic Hormone and Cortisone, Cortisone Investigator, No. 28, Nov. 1, 1951; Abstract 929.

The patient was discharged on Feb. 1, with vision of 20/50 in the right eye and 20/70 in the left eye without correction, or 20/40 — 2 in the right eye and 20/40 + 2 in the left eye with her own glasses. At this time the media were clear and the fundi greatly improved over their condition on admission. The disks were nearly normal; the edges were well seen; there was no elevation; a few resolving hemorrhagic areas were noted on and near the disk; the retinal vessels were normal; the maculae were normal; the peripheral portion of the retina was normal at all times; the blind spot was still slightly enlarged. A week later vision was 20/30 in each eye, and this was improved the following week to 20/20 — 2 in each eye (Fig. 4C) with new glasses. Since then the patient has had no further trouble, and up to the present time (five months after treatment) the corrected vision has remained 20/20 — 2.

COMMENT

The results in this case were highly favorable. Vision improved in a few days from less than 10/200 to 20/50 in each eye, and then rapidly to 20/20 with the proper refractive correction. The condition had responded only very slightly, if at all, to 1,600 mg. of cortisone, vision remaining below 10/200 in each eye, with no change at all for the last six days of the cortisone therapy. Chloramphenicol and nicotinic acid, likewise, seemed to have had no influence on the course of the condition. The subjective improvement was greatest on the third day of the intravenous use of corticotropin, and the patient's entire outlook literally changed overnight. One can, of course, draw no definite conclusions from one case, and it is fully realized that sudden remissions in this condition are part of the nature of the disease. It is my belief, notwithstanding, that the intravenous use of corticotropin did in this case materially contribute to the patient's return of vision. The reports in the literature on the treatment of optic neuritis with intravenous administration of corticotropin have been good, in contrast to the poor results obtained with cortisone. In some cases cognizance was taken of the tendency to spontaneous remissions in optic neuritis, and treatment was stopped as the patient improved to see whether a relapse would occur, as would be expected during the initial stage of treatment if the improvement was not spontaneous. McLean, Gordon, and Koteen [14] reported:

> . . . [In] a case of acute retrobulbar neuritis in which ACTH was given [the response was] . . . a prompt eosinophil drop, resolution of scotoma, and improvement in acuity. As the visual loss decreased, a placebo was substituted with a prompt rise in eosinophil count and recurrence of visual loss. On resumption of ACTH, improvement was resumed and it was maintained as the drug was slowly withdrawn when improvement was complete. We feel that this type of evidence is strongly suggestive of a drug-induced result and not coincident natural remission.

It is quite possible that, owing to the diversity of causes of optic neuritis, the condition will be found to respond in some cases, while in others it will not. Certainly, in a case in which the disease was probably on an infectious basis, viral perhaps, one might expect a favorable result. Other authors [13] have expressed the belief that healing is not accelerated until the eosinophile count has been depressed to the range of 0 to 50 cells per cubic millimeter. The present case seems to lend support to this view. Intravenous administration of corticotropin is undoubtedly a most valuable addition to the many other forms of therapy of optic neuritis, and in some cases may be spectacularly successful.

14. McLean, J. M.; Gordon, D. M., and Koteen, H.: Clinical Experiences with ACTH and Cortisone in Ocular Diseases, Tr. Am. Acad. Ophth. **55**:565-572 (May-June) 1951.

OBSERVATIONS ON VERTICAL DIVERGENCES AND HYPERPHORIAS

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THE VERTICAL prism vergences (variously called vertical fusional amplitudes and maximal vertical divergences) of most subjects are of the order of ± 2.5 to $\pm 3\ \triangle$.[1] With repeated or prolonged testing it may sometimes be possible to increase these limits a little.[2] Ophthalmologists usually regard this range of vertical prism vergences as implying fixed limits in the ability of neuromuscular apparatus and the fusion powers of the two eyes to make vertical divergences. Hyperphorias are considered of real significance so far as their magnitudes encroach upon these limits of divergence. Yet, clinically speaking, if small hyperphorias were thought to be the cause of symptoms, they were corrected by prisms, even though the vertical prism vergences were equal and normal.

In this paper it will be shown that the eyes of most persons are capable of compensating for, or adapting to, much larger degrees of vertical divergence. With this adaptation the same symmetrical and normal range of prism vergences, as well as the original hyperphorias, is maintained. A certain group of patients with concomitant hyperphorias, however, react very differently to vertical prisms in that no such compensation occurs.

The effect of prisms upon the vertical divergence of normal and non-normal eyes can be studied advantageously by means of the fixation disparity technique. With this method the "hyperphoria" is measured while the fusion of the images in the two eyes is maintained. This technique has been used in the experimental work to be described in this paper.

I. STUDY OF FIXATION DISPARITY IN THE VERTICAL MERIDIAN

Study of the fixation disparity in the vertical meridian follows naturally the study previously made by us [3] in the horizontal meridian. In the vertical meridian

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1. Fink, W. H.: Surgery of the Oblique Muscles of the Eye, St. Louis, C. V. Mosby Company, 1951, p. 260.

2. (*a*) Herzau, W.: Über das Verhältnis von erzwungener Vertikaldivergenz und Rollung bei der Fusion, von Graefes Arch. Ophth. **122**:59-74, 1929. (*b*) Ellerbrock, V. J.: Experimental Investigation of Vertical Fusional Movements, Am. J. Optom. **26**:327-337 (Aug.) 1949; (*c*) Experimental Investigation of Vertical Fusion, ibid. **26**:388-399 (Sept.) 1949.

3. (*a*) Ogle, K. N.; Mussey, F., and Prangen, A. deH.: Fixation Disparity and the Fusional Processes in Binocular Single Vision, Am. J. Ophth. **32**:1069-1087 (Aug.) 1949. (*b*) Ogle, K. N., and Prangen, A. deH.: Further Considerations of Fixation Disparity and the Binocular Fusional Processes, ibid. **34**:57-72 (May, Pt. 2) 1951.

one would expect the behavior of a fixation disparity, especially under the stress of forced vertical divergences, to be simpler than that in the horizontal meridian. The associative functions are not present in the vertical meridian to the extent that they are in the horizontal meridian.

Instrumentation.—Light patterns and special test details were projected by suitable lanterns on an aluminum-coated screen (Fig. 1) at 2.5 meters from the subject being tested. The subject observed the screen through a phorometer and through a pair of polaroid® plates. The planes of polarization of the light seen through these plates by the two eyes were at right angles to each other. These plates could be lowered out of the field of view or could be interchanged before the two eyes if desired. The target providing fusion stimuli, as projected by a lantern, consisted of a photograph of three Snellen charts placed side by side. The total visual field of details subtended an angle of about 20 degrees to the subject.

A small area with a visual angle of about 1.25 degrees to the subject was blanked out in the center of this target. This area therefore appeared black to the subject. Upon this small area a test detail consisting of a pair of nonius (vernier) lines was projected from a second lantern, in which a specially designed slide unit was fitted into the usual slide opening. The test

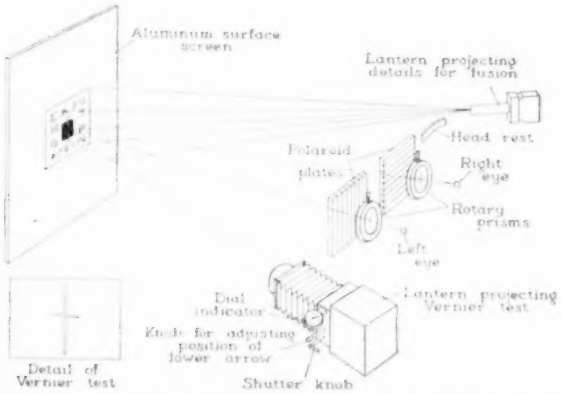

Fig. 1.—Sketch of apparatus used to measure fixation disparity in the vertical meridian.

detail consisted of a single long vertical bright line and a pair of opposing (vernier-like) short horizontal lines (Fig. 1). The light from these short lines was polarized by suitable polaroid® film on the slide arrangement. When seen upon the screen by the subject through the polaroid® plates, the short line on the right side was seen by one eye only; the line on the left side was seen by the other eye only. The one on the right was stationary, but the left line could be displaced vertically and adjusted by means of a knob and screw on the slide unit in the lantern. The angular vertical displacement of the left line relative to the right line, as measured to the eyes, could be read by the operator from an accurate dial indicator on the lantern to an estimated visual angle of 0.2 minute of arc. The left arrow could also be occluded or flashed on the screen at the will of the operator by means of a shutter. A light-green filter was also placed over the right (stationary) line in the lantern, so that the two lines could be identified more easily by the subject. The general illumination of the test room was kept moderately low, and the luminosity of the details on the screen was kept constant throughout the study. The binocular visual field was restricted wholly to the details projected on the screen.

To the phorometer were also attached special rotary prisms, so made that prismatic deviations could be introduced in the vertical meridian in steps of 0.25 △, with a precision of about 0.05 △.

Procedure.—After the subject's head and eyes were adjusted to the phoropter, the vertical (distant vision) hyperphoria was measured. A spot of light was projected on the center of the

screen with the room dark, and a Maddox rod was placed before one eye. The horizontal light "streak" caused by the Maddox rod was occluded to the subject and then exposed momentarily, after which procedure the subject reported whether the streak was higher or lower than the light spot. The operator then introduced a suitable vertical prismatic deviation by the rotary prisms until the light spot and the streak were superposed. This occluding procedure tends to eliminate voluntary alignment or any tendency on the part of the subject to "fuse" the images of the streak and the light spot.

With the details for fusion projected on the screen, the operator checked to be sure that the subject saw through the polaroid® plates only the right of the two nonius lines with the right eye, and only the left with the left eye. The subject was asked to look at the green (right) line. Then the operator exposed the left line briefly by means of the shutter and asked the subject to state whether he saw that line above, below, or level with the green one. By adjusting the displacement of the left line and obtaining the subject's response for each displacement, the operator could easily find the average position and limits of displacement within which the subject reported that the two lines appeared level. The actual displacement of the test lines is the fixation disparity, and this shows the actual vertical deviation between the visual axes of the two eyes while fusion is maintained. The displacement was recorded as a vertical angle subtended at the subject's eyes in minutes of arc. At the beginning of the test the "zero" for each subject was determined with the polaroid® plates lowered so that both eyes saw both nonius lines. Persons with normal visual acuity and an average discriminative sense can easily see a displacement of the two nonius lines measuring 1 minute of arc.

Data were taken while the subject wore his spectacles or when trial case lenses were used to correct any refractive error. The vertical deviation of the nonius lines, the fixation disparity, was first determined for this normal condition. The disparity was then determined for each of a sequence of forced vertical divergences caused by introducing equal but opposite prismatic deviations before the two eyes with the special rotary prism device in 0.5 △ steps. The forced vertical divergences in the sequence were alternated from a right hyperdeviation, or positive vertical divergence (prisms base down before the right eye, base up before the left eye) to a left hyperdeviation, or negative vertical divergence. This procedure was adopted in order to prevent a cumulative tonus in the ocular muscles. When the larger vertical prismatic deviations were first introduced, it was often found that a large vertical disparity would be measured. This decreased rather quickly, however, to a seemingly stable value in the course of 15 to 20 seconds. This reading when the eyes seemed to assume steady positions was taken as the final measurement. The measurements were continued for the sequence of larger and larger degrees of forced vertical divergences until the subject saw two images of the chart and fusion could not be maintained.

Results.—More than 65 subjects, the majority of whom were patients at the Mayo Clinic, were tested according to the procedure outlined. Typical data are shown graphically in Figure 2 *A* and *B*. The abscissas show the vertical divergence forced by the prisms (in prism diopters); the prism strength needed to force a right hyperdeviation (positive vertical divergence) is plotted to the right of the graph, and that needed to force a left hyperdeviation (negative vertical divergence) is plotted to the left of the graph. The ordinates show the corresponding vertical deviation of the visual axes of the two eyes as measured, that is, the vertical fixation disparity in minutes of arc. The values plotted above the origin show a right hyperdeviation (positive deviation); those below the origin show a left hyperdeviation (negative deviation). Inspection of the two graphs illustrates the fact that, in general, the data tend to fall on a straight line throughout the course of the forced vertical prism vergences.

These data show that when a positive vertical divergence is enforced, the pointing of the eyes actually "lags" behind this demand, because a negative fixation disparity, that is, a small left hyperdeviation, is measured. In other words, the eyes

do not make the full divergence movement demanded by the prisms; they "lag" slightly behind to the extent of the fixation disparity. When a negative vertical divergence is enforced, the deviation occurs in the opposite direction. This "lag" in eye position behind the vertical divergent positions of the images caused by the prisms was described by Hofmann and Bielschowsky [4] many years ago. It probably indicates a compromise between the strength of the compulsion to maintain fusion and the accustomed eye positions.

Tests show that these data are highly repeatable. They are therefore a characteristic of the subject being tested. In Figure 2*A* the data are for a subject whose

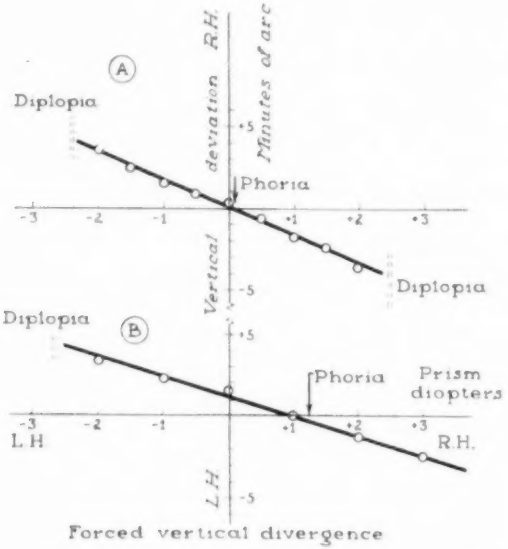

Fig. 2.—Graphic representation of typical measurements of fixation disparity in the vertical meridian when vertical divergences are enforced by prisms.

eyes are normally balanced in the vertical meridian. No fixation disparity exists under normal conditions, and the line that describes the course of the data intersects the abscissa essentially at zero. The hyperphoria measured for this subject was also essentially zero.

In Figure 2*B* data are shown for the eyes of a subject with a right hyperphoria of 1 to 1.5 △. There is a right hyperdeviation (positive vertical disparity) of about 1.5 minutes of arc, and the line that best describes the data points crosses the abscissal axis at about +1.0 △ of vertical divergence (prism base down before the right eye, base up before the left eye). This point of crossing indicates that for this vertical divergence the disparity has been made zero and therefore the muscle imbalance in the vertical meridian is exactly neutralized while fusion is maintained. The hyperphoria measured and the crossing point of the data line here agree reasonably well.

4. Hofmann, F. B., and Bielschowsky, A.: Über die der Willkür entzogenen Fusionsbewegungen der Augen, Arch. ges. Physiol. **80**:1-40, 1900.

Figure 3 shows the data on six subjects selected to illustrate types of curves found less frequently. The notations for abscissas and ordinates are the same as those of Figure 2. For the majority of subjects tested the data are the type shown in Graphs *A*, *C*, and *E*. Straight lines appear to describe the data except for such graphs as those in *B* and *D*. The slope of any of these lines is the regular change in fixation disparity for each prism diopter of enforced vertical divergence. The average range of the slopes for the subjects tested is between 1.5 and 1.9 minutes of arc for a change of 1 △ in forced vertical divergence. For more than 50% of

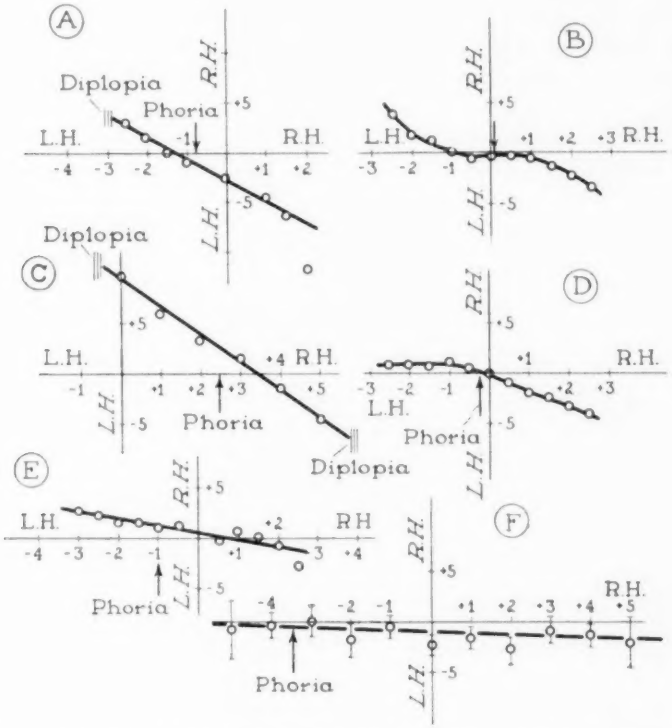

Fig. 3.—Selected cases of data showing variations in the type of graphs of fixation disparity with forced vertical divergences.

the subjects tested, the slopes of these best-fitting lines fell within these limits. The smallest slope was near zero; the largest was 6.5 minutes of arc for a change of 1 △. The difference in slopes of lines among subjects appears to be much less for the vertical fixation disparity tests than that for the horizontal fixation disparity tests.[ab]

Only occasionally will the measured disparity in the vertical meridian exceed 5 or 6 minutes of arc. In the horizontal meridian much larger deviations were common, and even usual when the forced vergence of the eyes was near the limits of convergence and of divergence. The size of Panum's areas of fusion is thought to be less in the vertical meridian than in the horizontal meridian, and this may account for the difference found.

In general the hyperphoria and that prism vergence which eliminates the disparity (the intersection of the best-fitting line and the abscissal axis) agree in direction and approximate each other in magnitude. Many exceptions occur, however. In making this comparison, one should bear in mind that frequently a hyperphoria may be modified by, or even be an artifact of, a lateral heterophoria as measured by disassociation tests, especially if that heterophoria is large. This effect is eliminated by the fixation disparity technique used here because fusion is maintained. Figure 4 shows a scatter plot of measurements of the hyperphoria and the corresponding vertical prism divergence which eliminates the fixation disparity. A correlation is evident from inspection. While the hyperphorias were measured within 0.25 △, one cannot expect the hyperphoria to be the same from time to time with quite this precision in all subjects.

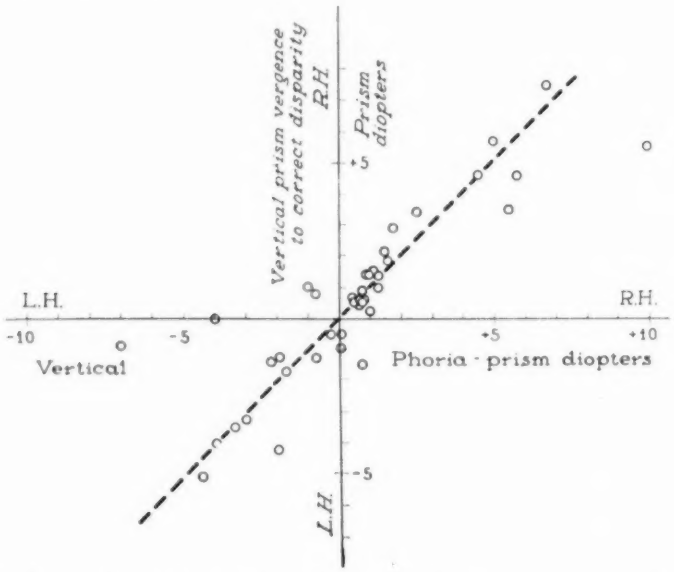

Fig. 4.—Scatter plot for hyperphoria and the prism divergence necessary to eliminate the fixation disparity.

For the vertical meridian we may assume, as we did for the horizontal meridian, that the fixation disparity is a manifest effect of opposition of the muscular tonicity, or innervational stress, involved in the synergy for vertical movements and the tonicity, or stress, from the compulsion to fusion. The latent vertical divergence of the eyes implied in this difference is held in check by synergistic tonicity. Yet the visual axes of the eyes can actually deviate by a small angle from correct pointing, and fusion of the images is maintained because they fall within Panum's fusional areas. When the eyes are forced into a vertical divergence by prisms by the fusion compulsion mechanism, they move into that divergence against the tendency of the muscles to maintain normal pointing of the eyes. This tendency to normal pointing offers the resistance to the forced vertical divergence. As the strength of this resistance increases, the fixation disparity increases. When this resistance is

equal to or greater than the maximal strength of the innervations from the fusion reflex, diplopia occurs.[3b]

Data on two subjects indicate that when the stimuli to fusion are restricted more and more to the periphery (by blanking out narrow strips horizontally in the center of the lantern slide that provides the details for fusion), the fixation disparity in the vertical meridian increases less rapidly than does the course of disparity in the horizontal meridian.[3a] This could be accounted for on the basis that the size of Panum's areas in the vertical meridian increases less rapidly toward the periphery than it does in the horizontal meridian. Shepherd [5] did not find the same increase of fixation disparity with peripheral fusion, even in the horizontal meridian, as we did.

Considerable interest would be attached to a study of subjects with double or alternating hyperphorias, for in the fixation disparity technique there is no loss of fusion and each eye has essentially the same task. Although Bielschowsky [6] stated that in a large percentage of subjects with heterophoria a double hyperphoria can be demonstrated, only one such subject was found in our study on hyperphoria. For this one subject the fixation disparity technique showed a right hyperphoria, in the direction indicated by the cover test. This was opposite that of the hyperphoria measured by the Maddox rod, which varied considerably from time to time, when that rod was placed before one eye and then before the other eye.

II. COMPENSATION FOR FORCED VERTICAL DIVERGENCES

A. Evidence for a Compensation.—If prisms were worn before the eyes to force a vertical divergence, one would expect the typical fixation disparity curve, as illustrated in Figures *2* and *3*, to be displaced along the abscissa an amount corresponding to the power of the prisms worn. This was not found to be true, however.

After the normal fixation disparity curve for a subject with essentially normal eyes had been obtained, prisms in fit-over frames, 1 △ base down before one eye, 1 △ base up before the other eye, over the usual spectacles (or in spectacle frames if there was no refractive error), were worn for two hours. The fixation disparity curve was then obtained while the subject still wore the prisms. The unexpected result was that the data obtained with the subject still wearing the prisms were nearly identical with those obtained before the prisms were worn. Figure 5*A* illustrates, typically, the results for one subject; the data are: those for (1) the normal and those obtained (*2*) after the enforced positive vertical divergence and (*3*) after the enforced negative vertical divergences produced by wearing prisms of 2 △. Figure 5*B* shows the same results when vertical prisms of 6 △ had been worn for two hours. These data show that the eyes have completely compensated for the deviation caused by the prisms. One line appears to fit all three sets of data. Of special interest is the fact that the vertical prism vergences are essentially the same for all three sets of data. Furthermore, the hyperphoria as measured with the Maddox rod (with prisms still before the eyes) was the same as that

5. Shepherd, J. S.: Study of the Relationship Between Fixation Disparity and Target Size, Am. J. Optom. **28**:391-404 (Aug.) 1951.

6. Bielschowsky, A.: Lectures on Motor Anomalies, Hanover, N. H., Dartmouth College Publications, 1940, p. 17.

measured before the prisms had been attached. Similar results were obtained on eight subjects with near-normal eyes. A search of the literature has shown that Schubert [7] is the only experimenter to have reported such a compensation. He used a heterophoria type of measurement and found that 2 △ of vertical divergence could be adapted for. However, Ellerbrock [8] also showed essentially this compensatory phenomenon in his study of the fusional movements, in which he used vertical prisms of 3 △.

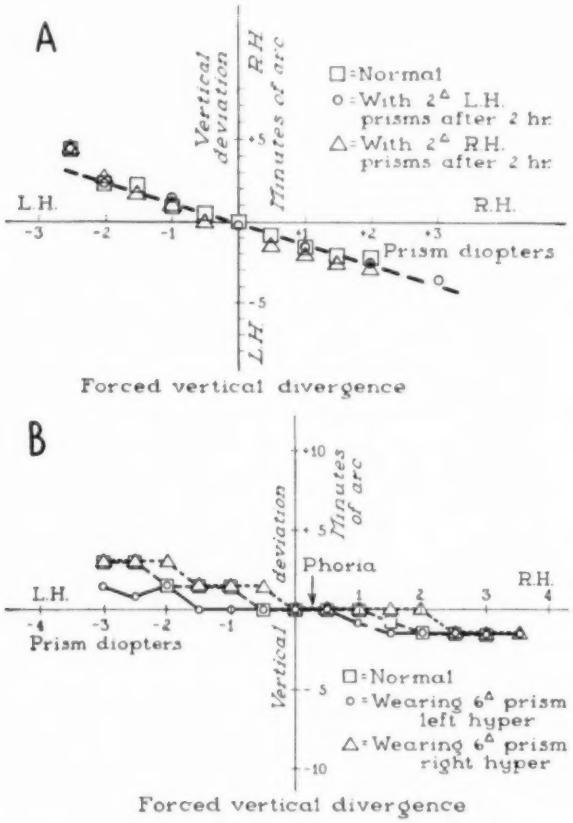

Fig. 5.—*A*, data showing that a vertical divergence of 2 △ is entirely compensated for while normal prism vergences are maintained. *B*, same as *A* except that 6 △ has been compensated for.

Because this compensation for vertical prisms was an unexpected result, the data obtained previously on many subjects were reviewed to see whether they contained hints of such a compensation. Possibly data such as *B*, *D*, and *F* of Fig-

7. Schubert, G.: Grundlagen der beidäugigen motorischen Koordination, Arch. ges. Physiol. **247**:279-291, 1943.

8. Ellerbrock, V. J.: Tonicity Induced by Fusional Movements, Am. J. Optom. **27**:8-20 (Jan.) 1950.

ure 3 illustrate in certain or all parts a rather rapid compensation for the vertical divergence during the elapsed time necessary to obtain the measurements. Data represented by lines with small slopes could be evidence of a rapid compensation. It was recalled also that in taking data when the larger vertical divergences were enforced by prisms, it was frequently found the first fixation disparity to be measured would be large, but that this always decreased to a seemingly constant value in the course of the 15 to 20 seconds required.

B. Rate of Compensation to Forced Vertical Divergence.—The next step was to study how rapidly this compensation to vertical prisms takes place. In this study it was found that for normal eyes prism vertical divergences of 6 △, and probably

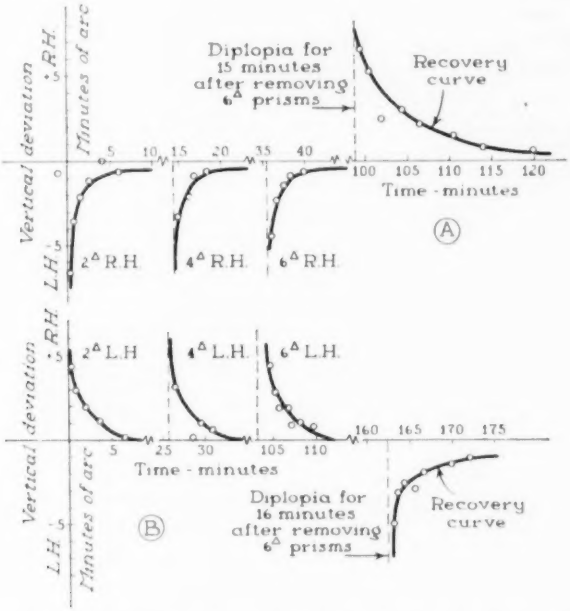

Fig. 6.—Fixation disparity data showing the rate at which vertical prism divergences can be compensated for and the rate of the recovery when the prisms are removed.

more, could be compensated for. This is certainly a greater vertical divergence than any to which compensation has heretofore been believed possible.

The procedure was first to measure the vertical fixation disparity and the hyperphorias with the eyes under usual conditions in order to establish the normal values. Then a 2 △ vertical divergence was introduced (1 △ base down before one eye, 1 △ base up before the other eye) by fit-over prisms, and the time of day was noted. The instant that fusion was reported by the subject, the fixation disparity was quickly measured, and again the time was noted. Measurements were then made at frequent intervals thereafter, the time being noted for each measurement. As the prismatic deviation was compensated for, the fixation disparity decreased. When this had reached the normal value, the prismatic deviation was increased by 2 △, making a total of 4 △ of vertical divergence. The same test procedure was then continued. When the disparity again reached the original value, the vertical prismatic deviation was increased to a total of 6 △. Again, the same test procedure was continued. When the disparity fell to its original

value, the measurements were discontinued, but the subject continued to wear the fit-overs 6 Δ for an hour or longer. The fit-overs were then removed. As soon as diplopia ended, the fixation disparity was measured at frequent intervals thereafter to determine how rapidly the eyes recovered from the previously forced vertical divergence.

A and *B* of Figure 6 illustrate the data for one subject for positive and negative forced vertical divergences respectively. These data show that under normal conditions when a vertical divergence is forced by prisms and there is fusion, at first a large hyperphoric muscle imbalance, as measured by the fixation disparity, occurs in a direction opposite that of the forced vertical divergence. As fusion continues to be maintained, however, this hyperphoric stress decreases and finally returns to its former level (the original hyperphoria). When this state has been reached, the prism no longer affects muscle balance between the two eyes. The eyes have fully adapted to the prismatic deviation. Inspection of the graphs shows that this particular subject completely compensated for the 2 Δ steps of vertical prisms in about six minutes after fusion was obtained. The greater part of the compensation occurred in the first few minutes. The time required for compensation in the seven subjects studied varied from 3 to about 10 minutes. The compensation curves in these charts can be adequately described by the same logarithmic curve.

When the fit-over prisms of 6 Δ were removed, diplopia set in for a period of 2 to 16 minutes, this time varying among the subjects. The magnitude of the fixation disparity measurement shows that even when fusion does occur, there is still a large hyperphoric stress between the two eyes. This stress is in the direction of the previously forced vertical divergence. Hence it appears that the eyes resist the new demand for a change in vertical divergence. This change is, in effect, as though a forced vertical divergence had been introduced from a "normal" position of the eyes, which in this case was in the direction opposite that of the prisms just worn.

The rate of recovery can also be represented by a logarithmic curve, but the time required for recovery is two or three times as long as that required in the original compensatory processes. Why this is so is not clear, for seemingly the same processes are involved. In fact, one might expect this recovery to be more rapid. The rate of recovery was sometimes different, depending on whether the forced divergence had been a left hyperdeviation (negative) or a right hyperdeviation (positive), indicating perhaps a natural hyperphoric tendency of the subject. The rate of recovery may, of course, also depend on the length of time that the 6 Δ prisms have been worn.

The phenomenon that prisms base down or base up before the eyes do affect the tonicity of the ocular muscles involved in vertical fusional movements is, of course, well known.[9]

Five of the seven subjects who wore the prisms experienced no particular ocular discomfort (even with the prisms of 6 Δ). Two of the subjects did feel some sort of a dull eyestrain with the prisms in one direction, but not in the other. All commented on a feeling that objects in space appeared queer. However, this

9. (*a*) Ellerbrock.[8] (*b*) Bielschowsky, A.: Disturbances of the Vertical Motor Muscles of the Eyes, Arch. Ophth. **20**:175-200 (Aug.) 1938. (*c*) Hofmann, F. B.: Physiologische Optik (Raumsinn), in von Graefe, A. C., and Saemisch, E. T.: Handbuch der gesamten Augenheilkunde, Berlin, Julius Springer, 1925, Vol. 3, Pt. 2, p. 309.

queerness could be due to the distortion of the prisms [10] rather than to the vertical divergence. Our result here does not agree with the reports of Herzau,[2a] of Eckardt and associates,[11] or of Wolff.[12] Eckardt and associates and Wolff found that one subject, while wearing prisms of 2 △ to produce a vertical divergence, experienced dizziness, slight nausea, and difficulty with concentration after 30 minutes. Since we do not know the vertical muscle balance for the subject tested in these reports, it is difficult to compare our results with theirs. Had our subjects worn the 6 △ prisms for longer than one to two hours, it is also possible that more positive symptoms of discomfort might have developed.

The rate of recovery from wearing prisms that force a vertical divergence is even much slower if simultaneous binocular vision is prevented during the period of recovery. Figure 7 shows such a recovery curve; the data for each curve are the hyperphoria measurements made from time to time after a total of 6 △ (divided between the two eyes) in fit-overs had been worn for about an hour.[13] At the

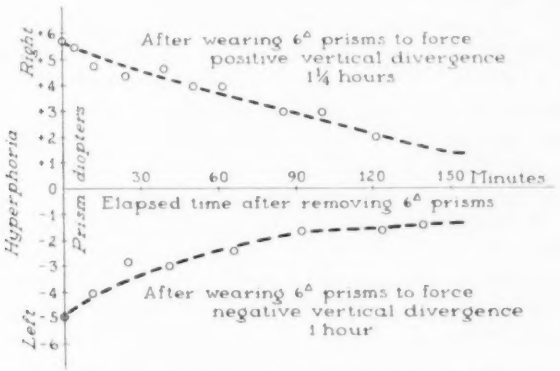

Fig. 7.—Hyperphoria measurements showing the rate of recovery from wearing 6 △ prisms for one hour when during the recovery binocular vision was prevented by an occluder.

beginning of the recovery test after the prisms had been worn for an hour, the hyperphoria measured was between 5 and 6 △ in the direction corresponding to that of the forced vertical divergence caused by the prisms. Thus, these data also show an almost complete compensation for the vertical prisms, as measured by the Maddox rod. Inspection of the curves shows that, in the absence of stimuli for fusion, the hyperphoria had not returned to normal even after 2½ hours. This result agrees with that reported by Schubert,[7] who, however, used only a total of 2 △. Bielschowsky,[6] Herzau,[2a] and others knew of this phenomenon in a general way.

10. Ogle, K. N.: Distortion of the Image by Ophthalmic Prisms, A. M. A. Arch. Ophth. **47**:121-131 (Feb.) 11952; Distortion of the Image by Prisms, J. Optic. Soc. America **41**:1023-1028 (Dec.) 1951.

11. Eckardt, L. B.; McLean, J. M., and Goodell, H.: Experimental Studies on Headache: Genesis of Pain from the Eye, A. Res. Nerv. & Ment. Dis., Proc. (1942) **23**:209-227, 1943.

12. Wolff, H. G.: Headache and Other Head Pain, New York, Oxford University Press, 1948, pp. 478-481.

13. It is, of course, impossible for most subjects to fuse the images when prisms of a total of 6 △ are introduced at once. The compensation for higher degrees of vertical divergence must be taken in steps of not greater than 2 △.

In view of these results, the trend of fixation disparities measured routinely with forced vertical divergences, as illustrated in the figures in this paper, may probably be an artifact of the elapsed time used to obtain each measurement. That is, if longer periods (minutes instead of seconds) had elapsed before a measurement for a given prism divergence was made, the fixation disparities would have decreased further toward the normal fixation disparity. The fact that approximately the same elapsed times were used for each measurement accounts for the highly repeatable data and the consistent trends of those data. Some subjects were able to compensate much more rapidly than others, and this fact is indicated when the fixation disparities are smaller and when the slopes of the lines that describe the data points are smaller. Still, the comparative slopes of the lines that describe the data points on the graph indicate the comparative strengths of the compulsion to fusion reflex. Likewise, the crossing point of the line on the abscissa still indicates the hyperphoria with fusion, and this is, of course, unaffected by the slope of the line or the time used for the measurements.

It must not be inferred from these data that 6 △ represents the maximal vertical divergence that can be compensated for. This divergence was merely the largest feasible in these particular experiments. For two of the seven subjects, however, 5 △ appeared to be the maximum when used to enforce a vertical divergence in one direction, but 6 △ was not the maximum for a forced vertical divergence in the other direction. Various data suggested that there was a tendency for the eyes of most subjects to be hyperphoric in one direction or the other, though measurements of hyperphoria or prism vergences in general did not disclose a muscle imbalance.

This compensation to prisms probably occurs also in the horizontal meridian. Schubert [7] reported such a compensation for prisms of 6 △ placed base out before the eyes. In our studies there were subjects for whom the fixation disparity in the horizontal meridian was unaffected by prisms over quite a range of forced convergence.[3] This problem will be studied further.

C. Compensation of Vertical Divergences by Patients Who Have Hyperphorias.—In the first section of this paper, it was found that the fixation disparity curves for subjects with a hyperphoria were displaced along the abscissa in the direction of the hyperphoria (Fig. 3, Graphs *A* and *C*). Subjects with essentially normal eyes, however, compensate for even larger degrees of forced vertical divergence than most of the hyperphorias found in patients.

What is the underlying factor here that prevents the subject from compensating for the hyperphoria?

Figure 8*A* presents the data for a patient whose vertical phoria as measured by the Maddox rod was 1.5 △ of right hyperphoria. The fixation disparity data show that the hyperphoric condition was nearer 2 △. The patient returned after wearing for four months a prismatic correction of 1.5 △. The fixation disparity data obtained with this correction are shown on the graph by the triangles. These data show that for this person the hyperphoria is essentially corrected by the prisms. The amplitudes (prism vergences) are now symmetrical and normal.

However, prisms do not always at first reduce the measured hyperphoria (or displace the fixation disparity curve toward the origin of the graph) in proportion to the prism correction. For example, Figure 8*B* shows the data of a patient for

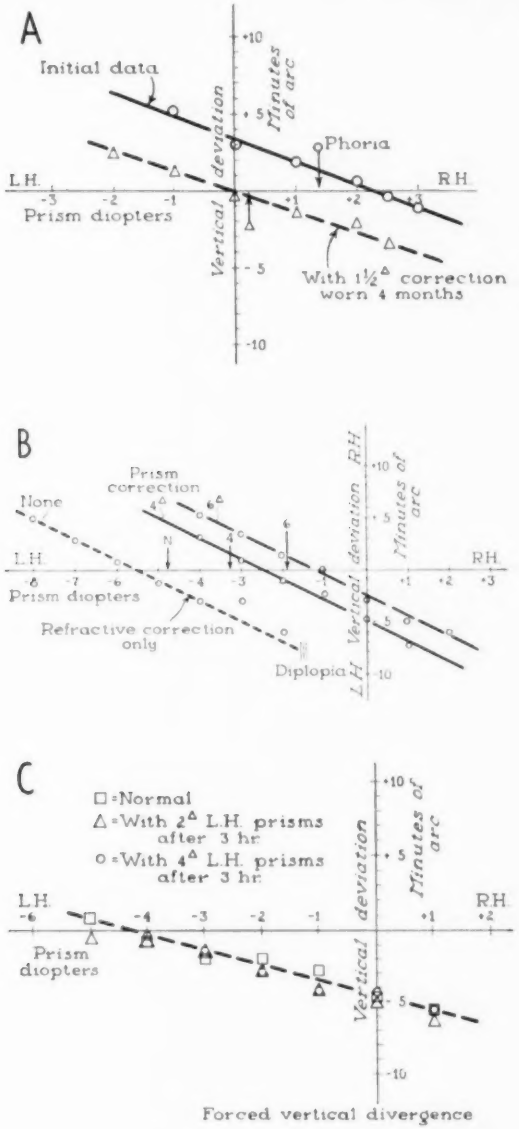

Fig. 8.—*A*, fixation disparity data for a patient with right hyperphoria that is corrected by vertical prisms. *B*, fixation disparity data showing a partial short-term compensation for prisms used to correct a hyperphoria. *C*, fixation disparity data for a patient with a large left hyperphoria that completely compensates for 2 and 4 Δ prisms prescribed. The initial hyperphoria, fixation disparity data, and prism vergences are maintained in spite of the vertical prisms.

whom the Maddox rod test, with refractive correction only, showed 4.75 △ of left hyperphoria. The fixation disparity curve shows that the prism divergence to eliminate the vertical disparity was near 5.5 △ of left hyperphoria. A fit-over frame with prisms, 2 △ base up before the right eye and 2 △ base down before the left eye, was attached to the spectacles. These the patient wore for two days. The fixation disparity data obtained then showed that the prism vergence to eliminate the disparity was 2.5 △, a change of only 3 △, whereas 4 △ had been given.

Then prisms for a total of 6 △ (divided between the two eyes) in fit-overs were attached to the spectacles. These the patient also wore for two days. The fixation disparity curve then measured while the patient still wore the fit-overs showed that the prism divergence to correct the vertical deviation was 1.25 △, a change of 4.25 △, instead of the 6 △ to be expected. Thus the effectivity of the prisms in each case when worn two days was about 70 to 75% of the prism power used. However, when this patient had worn for one month a 3 △ correction ground into her spectacle lenses, the fixation disparity curve showed more or less a 3 △ effect, in that the data line fell between the 4 △ and the 6 △ data lines of the graph. The hyperphoria was not entirely corrected, however, for 2.5 △ remained. Thus, this subject finally accepted the prisms to exactly the degree that was prescribed after they had been worn for a month.

In the two subjects whose data have just been described, the prisms corrected or partially corrected the optical effect of the hyperphoria. However, Figure 8C illustrates the fixation disparity of a patient for whom this was not true. The Maddox-rod measurement of the phoria was about 1.75 △ of left hyperphoria; the fixation disparity test showed that vertical prisms of 4 △ were necessary to eliminate the vertical fixation disparity. Fit-over prisms of 2 △ (divided between the two eyes) were attached to the patient's spectacles. These were worn for three hours. The fixation disparity data were then obtained with the patient still wearing the prisms. These data were identical with those obtained initially without the prisms. Even the hyperphoria measured was essentially the same as the hyperphoria first measured.

Then the prisms were increased to 4 △ (divided between the two eyes) and again attached to the spectacles in fit-overs. These were worn all afternoon and evening and part of the next morning. When the fixation disparity data were then obtained, with the patient still wearing the prisms, the measurements were found to be identical with those obtained previously. The left hyperphoria as measured with the Maddox rod was also essentially the same as that found initially, namely, 2 △. Thus, for this subject the vertical prisms did not correct the effective hyperphoria in the least. Instead, she compensated entirely for them. The data show that the original hyperphoria of the eyes has been maintained.

This result is rather startling. Yet it is only a more pronounced example of the data found for subjects having near-normal eyes who compensate completely to vertical prisms. For this patient a 3 △ vertical correction was prescribed. She reported by correspondence that she was having difficulty in getting used to the prismatic correction. Certainly, it is not unusual to find later the same hyperphoria in a patient with the prismatic correction that was prescribed to correct that hyperphoria.

It is probable that subjects such as the one whose data are illustrated in Figure 3*F* belong to the same group as those who compensate for vertical prisms. Here, however, the subject compensates almost immediately and almost completely for the prismatic deviations in the time required for the test. This subject compensated for both positive and negative vertical divergences of more than 5 △, and this in spite of a left hyperphoria of 3.5 △ that persisted. Throughout the data nearly the same small fixation disparity in the direction of left hyperphoria is measured. This subject reported no subjective symptoms of ocular discomfort.

D. Normal Demand for Vertical Divergences.—When a person uses his eyes in near vision, as, for example, in reading a newspaper, and, without his turning the head, looks toward an oblique point on the sheet, a vertical divergence between the eyes is necessary if fusion is to be maintained. Why this is so is illustrated in Figure 9. Let point *S* be the point of symmetrical convergence on the plane at a

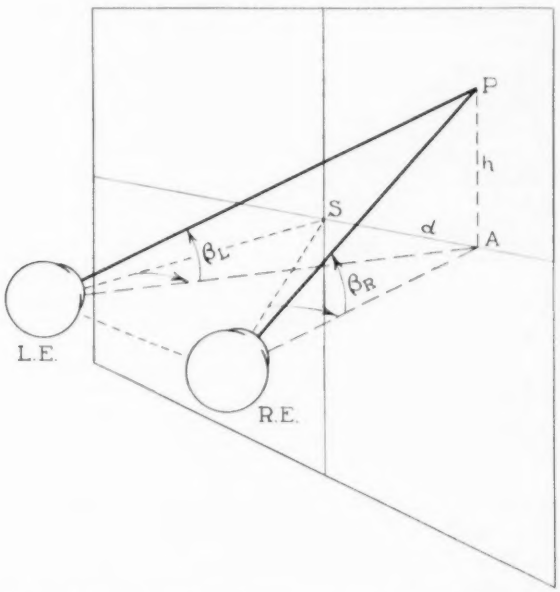

Fig. 9.—Sketch showing that vertical divergences are necessary when the eyes fixate an obliquely located point on a near plane.

near visual distance. If the eyes now turn to a point, *A*, in asymmetrical convergence, that point becomes nearer the right eye than the left eye. If, now, the eyes are raised to fixate the point *P*, the right eye must turn up through a greater vertical angle (β_R) than does the left eye (β_L). The distance *PA* subtends a larger angle to the right eye than it does to the left because the right eye is nearer *PA* than is the left eye. The difference in these angles of movement is the amount of vertical divergence that the eyes must overcome in order to maintain fusion. The magnitude of the forced vertical divergence, $\triangle = \beta_R - \beta_L$, will be greater the nearer the plane is to the eyes and the greater is the degree of obliquity and elevation of the point *P*. For more distant planes these vertical differences are negligible.

Nevertheless, as one reads a book or newspaper, different amounts and directions of vertical divergences are constantly being called into play as different parts of the page are fixated. One can easily calculate the vertical divergence geometrically. For an observation distance of 33 cm. and for a lateral angle of 24 degrees (15 cm.) to the right and for an elevation angle of 24 degrees (15 cm.) upward, a positive vertical divergence of 3 △ is required. This divergence is near the usually accepted limit for vertical prism vergence.

Now, hyperphoria measurements from points of light on a plane at 33 cm. do not show the 3 △ of hyperphoria to be expected on the basis of the geometric calculations. In fact, the data show no significant change in hyperphoria for any of the points on the plane. The accompanying Table gives for one subject the hyperphorias measured with a Maddox rod for a plane 33 cm. from the eyes, and for point sources of light at positions 15 cm. (24 degrees) to the right and to the left and 15 cm. (24 degrees) down and up. The center of the plane was located on the eye level of the subject and also was located for symmetrical convergence of the

*Results of Hyperphoria and Vertical Prism Vergences for One Observer, for Light Points on a Plane at an Observation Distance of 33 Cm.**

	Left 24° (15 Cm.)		Central		Right 24° (15 Cm.)	
	Hyperphoria	V.P.V.†	Hyperphoria	V.P.V.	Hyperphoria	V.P.V.
Up 24° (15 cm.)	0	+ 2.0 — 1.5	0	+ 2.25 — 2.0	0.25L ‡	+ 2.25 — 2.12
Central	0	+ 2.25 — 2.5	0.25L	+ 2.75 — 2.37	0.5L	+ 2.25 — 2.0
Down 24° (15 cm.)	0.5L	+ 1.62 — 2.75	0.5L	+ 3.0 — 2.5	0.62L	+ 2.25 — 2.25

* The data show substantially no hyperphoria and equal prism vergences for obliquely situated points, contrary to that to be expected on the basis of the geometry involved.

† V.P.V. indicates vertical prism vergence, in prism diopters; + values indicate positive vertical divergence (prisms base down for right eye or prisms base up for left eye); — values, negative vertical divergence (prisms base up for right eye or prisms base down for left eye).

‡ L indicates left hyperphoria, in prism diopters.

eyes. Care was taken that the head position remained the same and the eyes were on the same level. Similar results were obtained for three observers, none of whom were wearing refractive corrections. From these data we are forced to conclude that an immediate compensation must have been made for these geometric vertical divergences in the eye movements.

In the Table are also given the vertical prism vergences (vertical fusion amplitudes) measured with the point light sources at the four corners of the plane as stimuli for fusion. Larger objects for fusion stimuli at the oblique points were not used because of the difference in their angular sizes and shapes as seen by the two eyes. A special rotary prism calibrated in 0.25 △ steps was used. Inspection of the data in the Table shows that the vertical prism vergences at each of the four corners when fixated are normal and symmetrical, in spite of the geometric differences of 3 △ that should affect those divergences. Thus, the vertical divergence that has occurred here to correct the geometric difference is not just part of the amplitude of vertical divergence normally available, but, instead, represents a true compensatory divergence, independent of the normal vertical fusion ampli-

tudes. These data suggest, therefore, that an automatic compensation occurs in the coordinated vertical movements of the eyes, as the eyes are turned to fixate obliquely located points on a near plane.

COMMENT

We shall try to summarize the results just described, but shall include other evidence found in the literature and obtained from clinical experience. The following considerations are pertinent:

1. Unless there is some error in the reasoning in the preceding section, we must conclude that there is an immediate, and therefore reflex, compensation to the vertical divergences demanded by obliquely fixated points on a near surface. The normal vertical fusion amplitudes are not used to overcome these divergences, for the experiments show that normal fusional amplitudes (vertical prism vergences) are maintained while these points are being fixated.

2. In clinical tests vertical prism vergences are obtained relatively quickly (in seconds of time), and the limiting prism divergences of $\pm 3\,\triangle$ are usually found.

3. It would appear that the majority of subjects, whether having hyperphoria or not, have the ability to compensate for vertical divergences that are introduced by prisms of magnitudes certainly exceeding $6\,\triangle$. This compensatory process is a slower one than that in the clinical test, for it generally requires minutes of time to be complete. These larger degrees of vertical divergences caused by prisms can be compensated for only when the prisms are introduced in steps of about $2\,\triangle$, that is, in steps within the average range of clinically tested vertical prism vergence amplitude.

4. The hyperphoria measured on these subjects when the vertical divergences have been compensated for is usually the same as was the original hyperphoria, measured before the prisms were placed before the eyes.

5. Furthermore, we measure normal prism vergences (vertical fusion amplitudes) when these vertical prisms have been compensated for, these vergences being symmetrical about the new vertical divergence positions of the eyes caused by the prismatic deviation.

6. It is well known that many subjects who wear anisometropic refractive corrections show no hyperphoria (or the same hyperphoria) when the eyes are looking through the spectacle lenses in the primary position as when the eyes are looking through them in the reading position, in spite of the vertical divergence that is introduced by the difference in refractive powers of the lenses before the two eyes.[14] This fact can mean only that for many subjects the eyes are able to compensate immediately for the vertical prismatic deviations produced by spectacles. Moreover, in this case the prismatic differences vary with the direction of gaze of the eye, so that the compensation must be a constantly changing one.

7. Although perhaps a disputed point, the claim has nevertheless been made that nonconcomitant hyperphorias resulting from a paresis can after a short time become essentially concomitant. Such an occurrence would also involve a compensation not unlike that to vertical prisms. All eye movements are then executed

14. Cusick, P. L., and Hawn, H. W.: Prism Compensation in Cases of Anisometropia, Arch. Ophth. **25**:651-654 (April) 1941. Ellerbrock, V., and Fry, G. A.: Effects Induced by Anisometropic Corrections, Am. J. Optom. **19**:444-459 (Nov.) 1942.

normally with respect to a fixed hyperphoria. Hofmann [9c] suggested that when the fusional power works in one direction for a long time, it may be expected that adaptation will be more definite. It is even possible (Tschermak, cited by Hofmann) that an adaptation which is at first functional may later bring morphologic changes with it.

8. There are subjects with hyperphoria, however, who are not able to compensate for vertical prisms. These subjects will accept and maintain the prisms prescribed, and their effective hyperphorias [15] will be reduced in strict proportion to the prismatic deviation of those prisms. The effective hyperphorias of these subjects can therefore be corrected by prisms.

We might generalize from the preceding statements as follows: In the normal binocular activity of the eyes so far as vertical movements are concerned, there are compensatory or adaptive neuromuscular mechanisms that maintain a consistent coordination of the eyes, in spite of geometric differences caused by the particular position of points fixated in space and in spite of artificial obstacles introduced, such as prismatic deviation caused by anisometropic refractive corrections, or such as vertical prisms. However, these compensatory processes are independent of the original hyperphoria, for even after the prismatic deviation of vertical prisms has been compensated for, the original hyperphoria is found to be present.

Certainly, underlying these compensatory phenomena is the compulsion-to-fusion reflex, that reflex of the binocular visual apparatus that strives to direct the pointing of the eyes so that similar images fall as nearly as possible upon corresponding retinal points. However, to account for the compensatory phenomena described here there must be several constituents in this over-all reflex. We might picture the functions of these constituent reflexes so far as compensation to vertical prismatic deviations is concerned by such a chart as that shown in Figure 10. First, there are the two broad, or general, categories, in which the functions represented differ from each other in that the one controls the compensatory eye movements through a psycho-optical reflex (Hofmann [9c]) and the other controls the compensatory eye movements as a more nearly pure reflex—involuntary reflex, to distinguish it from the psycho-optical type. One might argue that the involuntary reflex is phylogenetically the older and the more basic of the two.

A psycho-optical reflex implies that a psychic factor is prerequisite to the initiation of the particular adaptive movements. Here, the psychic factor would probably be attention. The immediate compensation for the vertical divergences introduced geometrically by obliquely fixated points on a near surface, and the compensation of certain subjects for the varying prismatic deviations produced by anisometropic corrections are examples of this reflex. These psycho-optical adaptive reflexes must be looked upon as nonstabilizing (dynamic) in the sense that the changes for compensatory fusional eye movements are constantly being made to meet the immediate demands of the environment. Perhaps these are conditioned reflexes.

The second broad category, and that in which we are most interested in this study, pertains to those involuntary reflexes that must be responsible for the compensatory phenomena that one observes to vertical prisms. The reflexes in this

15. We use the term "effective hyperphoria" here to mean the hyperphoria measured when the subject is wearing the vertical prisms.

category are independent of any volition and result directly from optical stimuli alone. They are a direct function of the compulsion-to-fusion reflex, which tries to keep the images in the two eyes upon corresponding points. Usually the stimuli for these reflexes are artificial, since vertical prisms are not found in one's usual surroundings.

We divide this involuntary compensatory reflex for vertical prisms into two types in order to explain the compensatory phenomena described in this paper. The first pertains to the "rapid" adaptive vertical divergent movements of the eyes, as found in the clinical test for vertical prism vergences. In this test, the prismatic deviation is introduced relatively rapidly, and rather definite end-points are found beyond which diplopia exists. During this test the eyes tend to lag slightly behind the power of the vertical prisms used, the lag being greater the greater the vertical

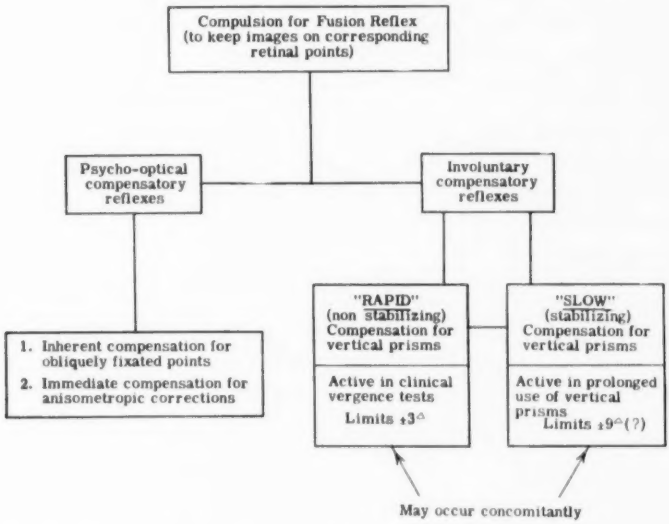
Compulsion for Fusion Reflex
(to keep images on corresponding retinal points)
Psycho-optical compensatory reflexes
Involuntary compensatory reflexes
1. Inherent compensation for obliquely fixated points
2. Immediate compensation for anisometropic corrections
"RAPID" (non stabilizing) Compensation for vertical prisms
Active in clinical vergence tests
Limits ±3△
"SLOW" (stabilizing) Compensation for vertical prisms
Active in prolonged use of vertical prisms
Limits ±9△(?)
May occur concomitantly

Fig. 10.—Possible categories of the compulsion-to-fusion reflex necessary to account for the phenomena described in this paper.

divergence. It is this "lag" of the eyes behind the vertical divergences of the prisms that is measured by the fixation disparity test. This fixation disparity measures, therefore, the hyperphoric status of the eyes during this comparatively rapid phase of adaptation during which fusion is maintained.

The second type of compensatory reflex, and the one in which we are most interested in this study, pertains to that ability of the eyes to compensate completely for vertical prism divergences, for divergences certainly exceeding 6△, if time is allowed. This is a "slow" process, requiring 3 to 10 minutes or longer, depending on the subject, before the eyes finally take vertically divergent positions corresponding exactly to the deviating power of the prisms used. Once the vertical deviation caused by the prisms is adapted to, further reflex eye movements are again normal in all respects relative to the newly adapted vertical divergent positions of the eyes. When the eyes are adapted to the prisms that force a vertical divergence,

the new (compensated) relative positions of the eyes become the natural ones, and constitute the base line from which all further normal eye movements are executed. Thus, this reflex must be a stabilizing one.

The normal fusional amplitudes measured clinically represent only the maximal divergences within which this slow stabilizing compensatory mechanism can begin to operate. It is for this reason that this slow compensatory stabilizing process must be considered separately from the "rapid" one that occurs in the usual tests for vertical divergence amplitudes. The slow process probably acts concomitantly, however, in the clinical tests for those vertical prism vergences. Its effect is usually negligible except when the test is prolonged, or except in certain subjects for whom this compensatory process might be more highly developed, and therefore faster, than that of the average subject.

Hoffman [6] knew something of this type of slow stabilizing compensation when he wrote:

> As soon as the mutual positions of the eyes are reached [in adaptation to a forced divergence], the prolonged fundamental tonus of the eye muscles forms the basis on which voluntary movements of both eyes are now set up. . . . [This process is] due to unconscious tonic but persistent (lasting) innervations to the eye muscles.

He, as did Schubert [7] later, and as is suggested in the present paper, distinguished these slow adaptive changes in eye positions from the customary "fusional movements," in the sense that the former are evidence of a "static" and the latter of a "dynamic" reflex phenomenon. From the time when Hofmann made the statement just quoted until the appearance of Schubert's paper little or no mention of these adaptive processes can be found in the literature.

On the hypothesis that the slow stabilizing, or involuntary, compensatory eye movements exist as a separate entity, one could argue that this slow component is nonoperative in those subjects who do not compensate for vertical prisms and that, accordingly, these subjects accept the prisms in exactly the degree to which they are prescribed.

The following problem must now be faced: Why should the hyperphoria persist and manifest itself independent of the compensatory processes? One might ask: Why cannot those subjects who are able to compensate for large vertical prisms also compensate for their own hyperphoria?

However, the circumstances under which a compensation can be made to vertical prisms—an objective stimulus to the compulsion-to-fusion reflex—may be different from those under which compensation could be made to a hyperphoria that is due to a motor obstacle or to an innervational anomaly to the muscles. When prisms are placed before the eyes, only the compulsion-to-fusion mechanism is essentially involved. It is true that when the prisms are first introduced an opposing hyperphoria occurs, presumably from the unaccustomed positions of the eyes; but this hyperphoria decreases under the compulsion to fusion until none (in the case of orthophoria) or the original hyperphoria remains. The hyperphoria in these subjects must be due either to a permanent mechanical anomaly or to a persistent unequal degree of innervation to those ocular muscles involved in the vertical divergence synergy or to both factors. These innervations persist in spite of, and in addition to, stimuli for vertical divergence corrective movements. If the hyperphoria is innervational, it is as though there were two centers for the control

of vertical divergences, the one controlling the slow and stabilizing compensatory mechanism and the other controlling the rapid and temporary compensatory mechanism. The innervational difference of the hyperphoria would affect only the second, or temporary, mechanism.

Another possible hypothesis for the persistence of a hyperphoria not of paretic origin or due to disturbances in the peripheral mechanism (basal nucleus, peripheral nerves, or orbital structures) lies in a possible difference in the optical distortion of the images of the two eyes or in the anatomic arrangement of corresponding retinal points in the vertical meridian. This possibility has, of course, been suggested before. Very schematically, we can illustrate this situation by Figure 11. Suppose the two eyes are observing a vertical ladder and both eyes are fixating the same middle rung *f*. The images of this rung then fall on the foveas of the two eyes. Suppose that for the left eye the images of all the rungs are equally spaced. For the right eye, suppose that the dioptric image is distorted or magnified unsym-

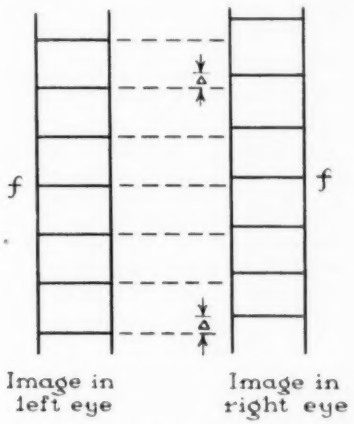

Fig. 11.—Figures to describe a hypothesis that could account for the persistence of a hyperphoria in spite of prismatic corrections.

metrically in the vertical meridian, such that the separation of the images of the successive rungs increases progressively above the fovea and decreases progressively below the fovea. Such an unsymmetrical type of magnification can be produced by a strong prism.[10] In binocular vision, except at the foveas, there would be a progressive increase in the vertical disparities between all the images in the two eyes for corresponding rungs, both above and below the fixated rung. These disparities are all in the same direction. They would constitute stimuli for a vertical divergence movement of the eyes, a divergence movement which tends to be held in c[illegible] by the fusion of the images of the center rung. Nevertheless, here would be a basi[illegible]r a persisting innervation for a vertical divergence, which in time could, conceiv[illegible]ly, become permanent. No prism correction could possibly eliminate the hyperphoria resulting from these innervations.[16]

16. We attempted to find what effect the type of distortion described here had upon fixation disparity. Before each eye was placed a pair of prisms, the first being a flat prism, the second a prism ground on a 9 D. base curve. The base of one was placed to the apex of the other,

(Footnote continued on next page)

These observations on hyperphoria and the relation of hyperphoria to vertical prism divergences may not satisfactorily account for the phenomena described in this paper. However, the ability of the eyes to compensate for vertical prisms is an important fact in ophthalmology. It would be of further importance to be able to distinguish between those subjects who will and those who will not respond to prismatic corrections, and between those subjects whose subjective symptoms of ocular discomfort are or are not truly due to hyperphoria.

SUMMARY

By means of the fixation disparity technique, hyperphorias were studied while the eyes were forced into vertical divergences by prisms. It was found that most subjects are able to compensate completely for vertical prism divergences certainly exceeding 6 △. When the divergence is so compensated, vertical prism vergences are still normal and symmetrical about the new positions of the eyes. For these subjects it was found, however, that the basic hyperphoria was maintained independent of the compensation. A certain group of patients with hyperphoria did not compensate for vertical prisms, but accepted those prisms in exactly the degree to which they were prescribed. It was shown that normally the eyes immediately compensate for vertical divergences required when the eyes fixate an obliquely located point on a near plane surface. This type of compensation was classed with that found in many subjects who wear anisometropic refractive corrections, in that the same effective hyperphoria is measured in all directions of gaze. Two components of the compulsion-to-fusion reflex are assumed in order to account for the compensatory phenomena. The first is psycho-optical. The second is involuntary and has two aspects, a rapid one, which is encountered in clinical prism vergence tests, and a slow one, which accounts for the complete compensation to vertical prism divergences. The problem of why hyperphorias persist in spite of the ability of the eyes to compensate for large vertical divergences is considered.

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the flat prism being nearest the eye. For each eye the prismatic deviations of the two prisms offset one another, but the greater, unsymmetrical magnification introduced by the flat prism remained.[10] The meridian of this unsymmetrical magnification was suitably oriented in the vertical meridian in both eyes. No consistent effect upon fixation disparity was measurable, but, of course, the periods of observation were relatively short and the strength of the prisms was only 3 △.

STRUCTURAL CHANGES IN CORNEAS OF GUINEA PIGS AFTER WEARING CONTACT LENSES

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WHEN A conventional contact lens is worn, the subject notes a haze or mistiness in his vision (Sattler's veil [1]), which can be shown to be due to corneal turbidity. Evidence has been produced indicating that contact lenses interfere with the normal water-removing function of the cornea,[2] which, being extraordinarily hydrophilic, tends constantly to imbibe water.[3] This water is continuously being removed, and recent experiments suggest that this is done, in part at least, by metabolic activity of corneal elements. Should this process fail, the cornea thickens [4] and becomes hazy.[5]

It appears unlikely that changes caused by contact lenses could occur without morphologic modifications. Corneal metabolism is based essentially on carbohydrates, and the epithelium, which normally contains much glycogen, is responsible for the major part of the total metabolic activity of the cornea.[6] It was thought that a histologic study of the cornea of animal eyes fitted with contact lenses would show the effect of such lenses on the corneal glycogen reserves, changes in corneal thickness, possibly the cause of corneal haze, and any marked increases in water content.

MATERIALS AND METHODS

Molds were made of the corneas of a number of guinea pigs, and contact lenses were fitted to them.[7] It was found that a number of other guinea pigs of the same size could be well fitted by these lenses. They were worn with a 1.5% solution of sodium bicarbonate ($NaHCO_3$) quite

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4. Kinsey, V. E.: An Explanation of the Corneal Haze and Halos Produced by Contact Lenses, Am. J. Ophth. **35**:691-695, 1952.

5. Smelser.[2] Smelser, G K., and Ozanics, V.: Importance of Atmospheric Oxygen for Maintenance of the Optical Properties of the Human Cornea, Science **115**:140-145, 1952.

6. Langham, M.: Utilization of Oxygen by the Component Layers of the Living Cornea, J. Physiol. **117**:461-470, 1952.

7. The contact lenses were made from these molds by the Obrig Laboratories, Inc., New York, and fitted by Mrs. M. Bergman, of that company.

comfortably for many hours without signs of irritation, such as conjunctival hyperemia, fluorescein-stainable damage to the corneal epithelium, or attempts by the animal to dislodge the lens.

Usually a contact lens was worn on one eye only, and the other eye was regarded as a control. At the conclusion of an experiment, the lens was removed, both eyes were examined for corneal haze with the aid of a bright beam of light in a dark room, and the animal was then killed.

The eyes were fixed in Bouin's solution, trinitrophenol (picric acid)-alcohol-formalin, or a freezing mixture of solid carbon dioxide and absolute alcohol.[8] This mixture was adopted because by this method it was hoped to immobilize and preserve the corneal components of glycogen, especially water, in the position occupied during life. The freezing, at about —79 C., was practically instantaneous throughout the very thin cornea (about 0.25 mm. in thickness), and the water was held at well below the melting point until dehydration had been completed, at —20 C. Absolute alcohol at this temperature slowly dehydrated the tissue; as this proceeded, the tissue components were fixed as the ice was dissolved, so that the water was at no time in a fluid state prior to dehydration. This method, admittedly, would not avoid formation and growth of ice crystals. The trinitrophenol (picric acid)-alcohol-formalin material was embedded and sectioned in paraffin, and that fixed in Bouin's solution, in pyroxylin. Corneas of the solid

Effect of Contact Lenses on Thickness of Corneal Stroma of Guinea Pigs

Time Contact Lens Was Worn, Hr.	Thickness of Stroma, μ	
	Left Eye: Control (No Lens Worn)	Right Eye: Experimental (Contact Lens Worn)
8	198	270
8	171	258
8½	162	216
8½	171	285
8½	192	294
8½	204	255
Mean	183	263

carbon dioxide-alcohol material were removed and dehydrated in absolute alcohol at —20 C. for three days and then embedded in pyroxylin. Control and experimental corneas were mounted in the same block, from which 8- and 10-μ sections were cut by the "dry" method. Ample time was allowed for infiltration and hardening of these blocks, so that tissue distortion was minimal and of the same degree in both the control and the experimental cornea.

RESULTS

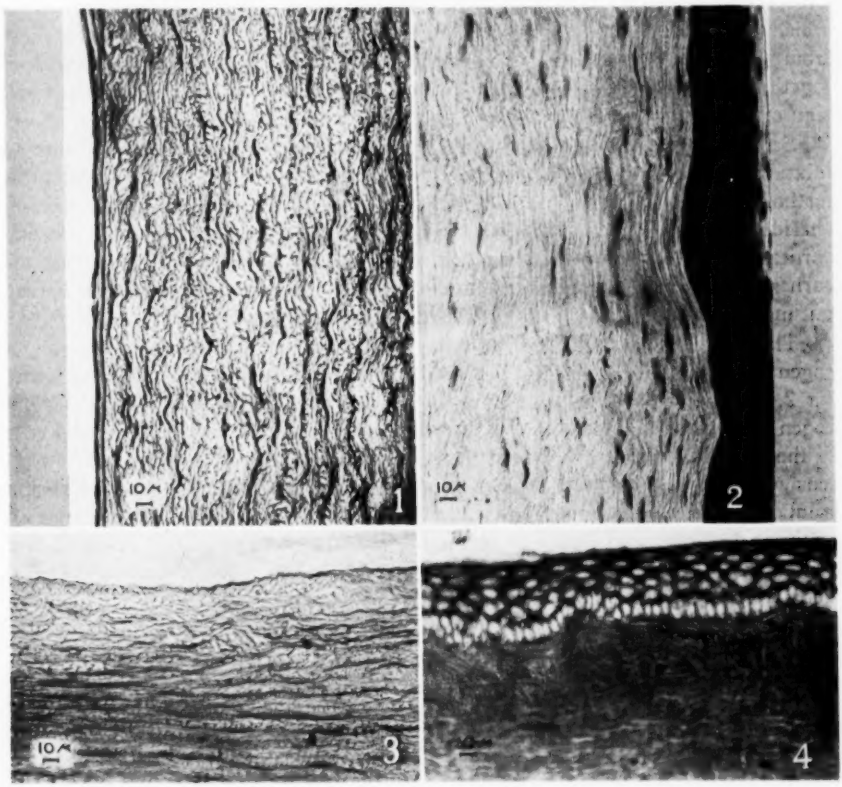
The corneas of 19 guinea pigs were studied. Contact lenses were worn from 30 minutes to 8½ hours, always with a 1.5% solution of $NaHCO_3$. A definite corneal haze resulted in all cases in which the contact lens was worn two hours or longer. A slight or questionable haze was noted in one case in each of the two groups in which the lenses had been worn 1 hour and 30 minutes respectively. At autopsy it was noted that the corneas of the contact-lens-fitted eyes were definitely thicker than those of the normal eyes. This was very noticeable in animals which had worn the lenses for the longer periods, as from six to eight hours prior to autopsy.

The first three eyes studied were those fixed in Bouin's solution and stained by routine methods. No obvious difference was noted between the experimental and

8. Friedenwald, J. S.; Scholz, R. O.; Snell, A., Jr., and Moses, S. G.: II. Primary Reaction of Mustard with the Corneal Epithelium, Bull. Johns Hopkins Hosp. **82**:102-120, 1948. Simpson, W. L.: Experimental Analysis of the Altman Technic of Freezing-Drying, Anat. Rec. **80**:173-189, 1941.

the control corneas, though careful measurements showed that the corneas of eyes which had worn contact lenses for 8½ hours were thicker in two of the animals.

The rest of the eyes which had worn the lenses from 2 to 8½ hours, fixed in the solid carbon dioxide-alcohol mixture and stained by routine methods, showed the most striking differences. The cornea which had worn a contact lens was in each instance thicker than the control cornea of the other eye. This increase in



1, section of guinea pig cornea after 8½ hours' wear with conventional contact lens. Solid carbon dioxide-alcohol fixation. Note separation of stromal lamellae by presumably water-filled spaces. The cornea is so increased in thickness that the epithelium does not show in this field. Compare with *2*.

2, section of a normal guinea pig cornea. Solid carbon dioxide-alcohol fixation. The stroma is fairly compact.

3, corneal epithelium of guinea pig after 8½ hours conventional contact-lens wear; solid carbon dioxide-alcohol fixation; modified Hotchkiss stain. Note distortion of stromal elements and absence of glycogen from epithelium. Compare with *4*.

4, normal corneal epithelium of guinea pig; solid carbon dioxide-alcohol fixation; modified Hotchkiss stain. Note compact corneal stroma and epithelial cells filled with glycogen.

stromal thickness averaged over 43% (Table) in those eyes which had worn the lens from 8 to 8½ hours. A similar increase in thickness occurred in the corneas of the animals which had worn contact lenses for four hours, but there was no

change in the half-hour experiments. No consistent change in thickness of the epithelium was found.

The increased stromal thickness was obviously due to apparently empty spaces between the corneal fibers and lamellae, so that the cornea appeared to be a meshwork (Figure, *1*). The holes were thought to represent spaces which in life were filled with water, and which may have been enlarged by growth of ice crystals which formed at the time of freezing fixation. Very likely they were, in part at least, artifacts, but they were very consistent and were found in all corneas of eyes which had worn contact lenses two hours or more prior to autopsy. Control corneas from the same animals, fixed and dehydrated in the same manner, embedded together and cut in the same block with the experimental corneas, did not show any sign of these water or ice-crystal spaces (Figure, *2*).

Sections of the corneas which had been fixed in the solid carbon dioxide-alcohol mixture were also stained by the periodic acid method of Hotchkiss.[9] With this method the corneal stroma stains a deep pink, presumably because of its polysaccharide content. The depth of staining of the corneal stroma of the experimental corneas was consistently less than that of the normal controls. The fact that the corneas were swollen, and the same amount of stainable substance was thus spread out more widely, could account for this difference.

This procedure stains a saliva-soluble material in the corneal epithelium (glycogen) very intensely. The corneal epithelium of the eyes wearing contact lenses for 2, 4, 8, and 8½ hours prior to autopsy were almost completely devoid of glycogen (Figure, *3*), compared with the normal (Figure, *4*). A few epithelial cells of the cornea near the limbus contained some glycogen after two hours of contact-lens wear. Corneas of two animals were fixed in trinitrophenol-alcohol-formalin solution and stained in the same manner. These also showed complete depletion of the corneal glycogen under the contact lenses. The glycogen store was not clearly reduced after 30 minutes of contact-lens wear, but in two animals studied after one hour some reduction in epithelial glycogen was apparent. In both cases glycogen in the basal layers of the epithelium was lost first, possibly indicating the greater lability of the substance in this region.

COMMENT

The corneal haze, which is induced in man when contact lenses are worn, is also produced in guinea pigs by such lenses, and when the lenses are worn with the same solutions that are commonly used clinically, this corneal turbidity is produced in approximately the same length of time. This haze is accompanied by pronounced changes in the histologic structure of the cornea. The increase in thickness of the human cornea which results when such lenses are worn also occurs in the animal experiments and is due to imbibition of water by the corneal stroma. The corneal epithelium does not appear to take part in this swelling, as its thickness varies in these experiments.

The water imbibed by the stroma was found to lie between the fibers throughout the entire cornea. The actual condition of this water cannot be determined on the basis of the current experiments—either the size of its droplets or its chemical

9. Hotchkiss, R. D.: A Microchemical Reaction Resulting in the Staining of Polysaccharide Structures in Fixed Tissue Preparations, Arch. Biochem. **16**:131-141, 1948.

relation to the corneal ground substance. It appears doubtful whether the corneal fibers themselves are swollen; however, they are grossly displaced and the lamellae separated. This disturbance of the orderly arrangement of the fibers, together with the probable change in the refractive index of the interfibrillary substance, appears to be an adequate explanation for the corneal haze induced by contact lenses. The transparency of the normal cornea is thought to be dependent on the maintenance of both the regular arrangement of the fibers and the refractive index of the interfibrillar material.[10]

These changes were not observed in preparations made after the use of ordinary fixatives, probably because they tended to shrink the tissue and cause collapse of the water spaces, thus concealing the changes. The use of a solid carbon dioxide-alcohol freezing mixture is thought to preserve this condition better because the water is held in place frozen and the tissue fixed slowly, without any considerable shrinkage as the ice is dissolved out by the alcohol.

Glycogen depletion of the corneal epithelium was a striking phenomenon and occurred concomitantly with the development of corneal haze and stromal edema. It is clear from the experiments of Cogan [3] and of von Bahr [11] on the swelling properties and thickness of the cornea that this tissue imbibes water very readily. It is known that contact lenses cause an increase in corneal thickness and changes in its optical properties in man, and it is thought that a disturbed water balance is responsible. Experiments have shown that an adequate oxygen supply will prevent these changes and that exclusion of oxygen from the cornea will induce them. This leads us to believe that a metabolic process is involved in water regulation in the cornea, with the energy required for this process very likely furnished by the glycogen stores. If, as indicated in earlier experiments,[5] anaerobic conditions exist under a contact lens, the metabolic work required would use the glycogen stores at a much greater rate than normal. The present experiments on guinea pigs indicate that they are used even more rapidly than they can be replaced. When the glycogen reserve has been exhausted, water enters the cornea more rapidly than it can be removed, and the cornea consequently swells and becomes hazy, owing to the accumulation of this water in the interfibrillar spaces.

It is not known whether the "halos" seen by contact-lens wearers are produced in animals by similar lenses. The "halos" could be caused by diffraction particles in the cornea, of about 16 μ,[12] or possibly by the connective tissue fibers acting as a diffraction grating. Since these corneal fibers are found to be separated by a fluid which probably has an index of refraction different from normal, this possible cause of the diffraction halos should not be discarded. The histologic preparations indicate that the interfibrillar fluid may be held in minute pockets or droplets, which could also act as diffracting particles. However, the size of these droplets is very variable, and one cannot be sure how much of a role formation and growth of ice crystals may have played in the production of the spaces seen in *1* of the Figure.

10. Caspersson, T., and Engström, A.: Hornhinnevävnadens transparens, Nord. med. **30**: 1279-1282, 1946.

11. von Bahr, G.: Measurements of the Effect of Solutions of Different Osmotic Pressure on the Thickness of the Living Cornea, Tr. Ophth. Soc. U. Kingdom (1948) **68**:515-524, 1949.

12. Finkelstein, I. S.: Biophysics of Corneal Scatter and Diffraction of Light Induced by Contact Lenses, Thesis, Columbia University, 1951.

The sequence of metabolic events which lead to the actual water removal are unknown. It is probable that water itself is not excreted, but that the active transfer of some electrolyte provides a more plausible mechanism. The site of this transfer or the cells which do the work are unknown. The work of von Bahr indicates that both the epithelium and the endothelium may engage in this activity. The relation of epithelial glycogen to this process, as shown in these experiments, directs one's attention to the epithelium. However, this tissue may act as a storehouse for the energy required, rather than being responsible for the actual transport.

CONCLUSIONS

The conventional type of contact lens fitted to guinea pigs produces a corneal haze similar to that produced in man. This change occurs in about the same time as in man when the same solutions are employed. Associated with the turbidity is an increase in corneal thickness, which has also been shown to occur clinically.[4] This increase is due to thickening of the stroma, but not of the epithelium. The stromal swelling is seen histologically to be due to separation of the lamellae and connective tissue fibers by spaces which in life were presumably filled with water.

The glycogen stores of the corneal epithelium are rapidly exhausted when contact lenses are worn. Reduction in epithelial glycogen occurs prior to pronounced corneal edema, swelling, and haze. The relation of these structural changes to corneal turbidity, Sattler's veil, and the "halos," or rainbows, experienced when contact lenses are worn is discussed.

Registry of Interesting Cases

It is the purpose of this section to record cases on the basis of interest only. No complete review of the literature is attempted and no claim for priority is implied except when specifically stated. Publication of case reports is subject to the concurrence of the Editorial Board on the interesting aspects of the case. It is requested that the reports submitted be as brief as is consistent with inclusion of the pertinent facts, bear a title that is as specific as possible, be prefaced by a paragraph that states why the author feels the case is of interest and be accompanied with photographs whenever possible.

GLAUCOMA ASSOCIATED WITH KRUKENBERG'S SPINDLE

A young patient with no complaints except refractive error was found to have Krukenberg's spindle, and a water-drinking provocative test for glaucoma gave a strongly positive result. The diagnosis of pigmentary glaucoma must be considered probable.

D. E. B., a man aged 21, was seen with a complaint of blurring of vision for distance, which was not completely corrected by his present lenses.

Refraction revealed low-grade myopia with astigmatism.

On ophthalmoscopic examination, some haze of the right cornea was noted, and slit-lamp examination showed a typical vertical, Krukenberg spindle, 5 mm. in length, on its posterior surface. A few pigment spots were seen on the left cornea, but not enough to form a spindle. The irides were blue-gray and showed minimal signs of atrophy.

After a tension reading (Schiøtz) of 25 mm. Hg in the right eye and 20 mm. in the left eye, 1 liter of water was taken on an empty stomach. One-half hour later the patient complained of haloes and blurring of the right eye. The tension was found to be 40 mm. Hg in the right eye and 32 mm. in the left eye. The pressure subsided to normal promptly on the instillation of pilocarpine.

The peripheral fields were normal as determined with a 3/330 mm. test object. Central fields, determined with 3/1000 and 1/1000 test objects showed normal physiologic blind spots and no other scotomas.

Gonioscopy showed a wide angle with no synechia. There was fairly heavy deposition of pigment in the angle.

Repeated measurements have never revealed a tension greater than 25 mm. Hg at any other time. However, detailed questioning after these studies revealed that mild haloes had been seen on a few occasions in the right eye, but no attention had been paid to them.

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Annual Reviews

DISEASES OF THE UVEAL TRACT

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IMPORTANT articles on diseases of the uveal tract are reviewed. Those publications appearing between October, 1951, and October, 1952, are included. A number of papers of possible importance were not obtained in time to be included, but will be incorporated in a subsequent review.

CONGENITAL DEFECTS

According to Ingalls, Tedeschi, and Helpern,[1] evidence has been presented to the effect that retrolental fibroplasia is basically the equivalent of a congenital defect of the human fetus. After exposure of pregnant mice to rarefied atmospheres a variety of skeletal and soft-tissue malformations were observed. In the eye a number of malformations were observed, including open eye (defective formation or premature separation of the eyelids), inward folding of the retina, reduction in size of the vitreous, forward displacement of the lens, and detachment of the hyaline capsule from the lens fibers. In the uveal tract, the iris and ciliary body showed no deviation from normal, but the choroid had lost its usual smooth curvature and showed an abnormal budding of proliferated cells. It is known that similar anomalies in rats and mice can be produced by exposure of the pregnant females to the toxic effects of trypan blue and x-rays and by induction of vitamin deficiencies. The authors emphasize a point which may be of value in future prevention of ocular anomalies. They state that some defects in rodents, which are primarily attributable to the action of a gene, may owe their secondary development to incompatible blood groups, as do some defects in human beings.

Uveal colobomatous defects may be associated with other anomalies, and appear in a great variety of forms. A case is reported[2] in which the child had bilateral coloboma of the iris, ciliary body, lens, choroid, and optic nerve. This anomaly occurred without a family history of a similar lesion. In another case[3] a 10-year-old girl exhibited a typical parapapillary coloboma of the choroid associated with a scotoma occupying all the upper field and connected with the blind spot. Gualdi[4] describes the case of a man aged 58 who presented a typical congenital coloboma

From the Francis I. Proctor Foundation for Research in Ophthalmology, University of California Medical School.

1. Ingalls, T.; Tedeschi, C. G., and Helpern, M. M.: Congenital Malformations of the Eye Induced in Mice by Maternal Anoxia, Am. J. Ophth. **35**:311-329 (March) 1952.

2. Guerra Grande, J. M.: Bilateral Coloboma of the Iris, Ciliary Body, Lens, Choroid, and Entrance of the Optic Nerve, Arch. Soc. oftal. hispano-am. **11**:1391-1395 (Nov.) 1951.

3. Gallo, A., and Borges-Vieira, B.: Typical Coloboma Simulating Supernumerary Papilla, Ann. ocul. **185**:268-272 (March) 1952.

4. Gualdi, G.: Typical Coloboma of the Choroid of One Eye and of the Iris of the Other: Report of a Case, Bull. Soc. med.-chir. Modena **51**:97-104 (Feb.) 1951.

of the iris associated with a congenital cataract in the right eye, and a coloboma of the choroid in the left eye. Eicke [5] and Czukrász [6] describe five cases of atypical coloboma of the iris.

Šakić [7] presents the report of a unilateral congenital anomaly consisting of large areas of atrophy of the iris stroma, obliteration of the angle of the anterior chamber by white mesodermal tissue, and secondary glaucoma. The white tissue in the chamber angle occupied over half the circumference of the eye. Wagner [8] describes the persistence of the fetal pupillary membrane in a child. This anomaly had previously been described in members of three generations of the same family. The membrane coalesced with the lens capsule, and both lenses showed diffuse subcapsular clouding. Bruce [9] presents the case of a 2-month-old boy who exhibited a pinkish-white tumor in the iris at from 7 to 9 o'clock in the left eye. The tumor was removed, without recurrence or sequelae. Pathologic studies showed aberrant glandular tissue in the iris stroma, presumably lacrimal gland tissue. Sun [10] describes a case of bilateral congenital aniridia in a young Chinese girl. The author points out that with the help of the slit lamp or gonioscope it is usually possible to demonstrate a short stump of iris tissue lying behind the corneoscleral margin, thus accounting for the development of glaucoma in cases of this defect. Jaffe and Knie [11] report a case of true polycoria. True polycoria may be said to exist when each pupil in an eye manifests a sphincter mechanism. This condition is rare, only four previous cases having been reported. Pseudopolycoria, however, is of frequent occurrence. In the case reported by these authors there were two pupils in the right eye, bilateral anterior polar cataracts, corneal opacities, and alternating hyperphoria. Each pupil in the right eye reacted normally to the usual stimuli and drugs. Vail and Merz [12] present the interesting case of a student nurse aged 21 who exhibited a peculiar pigmented elevated lesion lying in or under the iris stroma on the temporal side of the left eye. The lesion increased in size over a period of two months, and the eye was enucleated, with a diagnosis of malignant melanoma. Pathologic examination showed multiple cysts of the iris and ciliary epithelium. It was the opinion of the authors that these cysts were embryonic in origin and developed at about the 110-mm. stage. At this time the zonular membranes are fully developed and extend from the lens surface to the valleys and lateral surfaces of the ciliary processes. The ciliary processes and folds lie in close contact with the equator of the lens. As development proceeds from this stage onward, the distance

5. Eicke: Report on Three Pigmentary Cysts Seen in the Anterior Chamber, Klin. Monatsbl. Augenh. **119**:293-297, 1951.

6. Czukrász, I.: Data Concerning Atypical Coloboma of the Iris, Ophthalmologica **122**:53-57 (Jan.) 1951.

7. Šakić, D.: A Case of Dysgenesis Mesodermis Corneae and Iridis (Rieger), Ophthalmologica **123**:31-39 (Jan.) 1952.

8. Wagner, F.: Persistent Pupillary Membrane, Klin. Monatsbl. Augenh. **119**:580-585, 1951.

9. Bruce, G. M.: Aberrant Glandular Tissue in the Iris, Tr. Am. Acad. Ophth. **56**:47-51 (Jan.-Feb.) 1952.

10. Sun, K. Y.: Congenital Aniridia: Report of a Case, Chinese M. J. **69**:495-496 (Nov.-Dec.) 1951.

11. Jaffe, N. S., and Knie, P.: True Polycoria, Am. J. Ophth. **35**:253-255 (Feb.) 1952.

12. Vail, D., and Merz, E. H.: Embryonic Intra-Epithelial Cyst of the Ciliary Processes, Tr. Am. Ophth. Soc. **49**:167-183, 1951.

between the ciliary processes and the lens becomes greater. Any undue traction or pull by the zonule on the inner layer of the cup could readily reopen the space between the two layers and allow cyst formation.

ANATOMY AND HISTOLOGY

Vrabec [13] studied the endothelium on the surface of the human iris by a relief technique. Irises from the 7-month stage of fetal life to full maturity were examined. Flat, endothelial-like cells were found to cover the surface during fetal life. At the age of one year they seemed to become transformed into cells resembling fibroblasts, which, however, remained immature. The observation of reticular fibers in the anterior border layer of the iris seemed to confirm this transformation.

Ashton [14] studied flat and bulk preparations of choroid in which he injected "neoprene" to investigate the possible existence of arteriovenous anastomoses, or shunts, and to determine whether they possessed a glomus-like apparatus. The glomus consists of an afferent artery and an efferent vein and serves to control passage of arterial blood directly into venules, thereby bypassing the capillary bed. The shunt is enclosed by several layers of small polyhedral, epithelium-like cells, uniform in size, and with a well-developed cell membrane. These cells are intimately associated with nonmedullated fibers. By their contractility these cells control the blood flow through the shunt. The author was unable to demonstrate arteriovenous anastomoses in the large and medium-sized choroidal arteries with his technique. He was also unable to find glomus cells in the sections examined from 500 eyes.

Vilstrup [15] injected plastic compounds intravenously in living animals, removed the choroid from the eyes, and weighed it. After digestion of the tissues from the plastic and further weighing, he came to the conclusion that three-fourths to four-fifths of the total weight of the choroid was made up of its vascular contents. Employing a similar technique, he found that histamine-treated choroids weighed three to four times the choroids of the control animals.

DEGENERATIVE DISEASES

Essential Progressive Atrophy of the Iris.—Carter [16] reports a case of this condition in a 36-year-old housewife. Eight and one-half years after onset of the disease secondary glaucoma appeared and was not controlled by antiglaucoma medication or surgery. The author shows that the trephining operation failed because of overproduction of episcleral scar tissue. Löhlein [17] reports an unusual case in which the disease was bilateral. In both eyes the typical iris atrophy was present and secondary glaucoma developed. Van Beuningen [18] reports two cases of progressive

13. Vrabec, F.: Endothelium of the Anterior Surface of the Human Iris, Ophthalmologica **123**:20-30 (Jan.) 1952.

14. Ashton, N.: Observations on the Choroidal Circulation, Brit. J. Ophth. **36**:465-480 (Sept.) 1952.

15. Vilstrup, G.: Studies on the Vascular Capacity and Tissue Fluid Content of the Choroid and Their Variations Under Treatment with Histamine, Acta ophth. **30**:173-180, 1952.

16. Carter, L. F.: Progressive Essential Atrophy of the Iris: Case History with Pathologic Report, Am. J. Ophth. **35**:522-526 (April) 1952.

17. Löhlein, H.: Essential Progressive Atrophy of the Iris with Formation of a Hole and Glaucoma, Klin. Monatsbl. Augenh. **118**:379-388, 1951.

18. van Beuningen, E. G. A.: Comparative Gonioscopic Studies of Progressive Defects of the Iris, Klin. Monatsbl. Augenh. **119**:279-286, 1951.

unilateral localized atrophy of the iris. The 11-year-old girl presented an open angle, whereas the 46-year-old woman had closure of the angle by synechias, and glaucoma developed. Huerkamp [19] reports two cases of progressive atrophy of the iris which occurred in conjunction with xeroderma pigmentosum. He states that five previous cases of this condition have been reported in the literature. In these cases the lower portion of the iris was the more involved, suggesting that light also plays an important part in development of the ocular lesions.

Iridoschisis.—This condition occurs most commonly after the age of 55. It is characterized by splitting and separation of the anterior from the posterior portion of the iris. Fibrillar shreds are formed, which float in the aqueous and are attached toward the root of the iris. Cataract and secondary glaucoma are common in cases of progressive type. The condition is usually bilateral. Haik and associates [20] report such a case and suggest that the condition is a selective degenerative disease of the iris and, at times, of other ocular tissues. They are of the opinion that the degenerative changes arise on a basis of vascular occlusion. Chang [21] and Blegvad [22] report similar cases.

Familial and Hereditary Degenerations.—Ashton and Sorsby [23] report the clinical and pathologic findings in a case of an unusual dystrophy of the fundus. The earliest changes occurred in the retina and were characterized by an acute onset. Scarring, sclerosis of the choroidal vessels, and pigment proliferation followed. Microscopically, the choroid showed extensive atrophy with vascular sclerosis. The choriocapillaris was absent posteriorly and was atrophic anteriorly. Bruch's membrane was moderately and uniformly thickened and showed fine breaks, through which a serous fluid diffused. This fluid was organized by tissue from the choroid, and the pigment epithelium became disorganized. The outer layers of the retina were replaced by glial tissue, and the inner layers were adherent to hyalinized vascular masses, which lay beneath the retina. Because of the pathologic findings, the lesion was thought to be primarily choroidal.

Streiff and Portmann [24] describe the occurrence of angioid streaks and pseudoxanthoma elasticum in five siblings of a generation containing 13 members. Adelung [25] reports a similar case and states that mechanical factors, such as pressure on the eye, injuries, and accommodation, exert tension on Bruch's membrane and may result in the fractures which produce the observed fundus picture. It was suggested that abolition of accommodation might prevent progression of the lesions.

19. Huerkamp, B.: Atrophy of the Iris in Xeroderma Pigmentosum, Klin. Monatsbl. Augenh. **119**:286-292, 1951.

20. Haik, G. M.; Wood, L., and Waugh, R. L.: Iridoschisis: Report of Additional Case, A. M. A. Arch. Ophth. **48**:40-43 (July) 1952.

21. Chang, L. W.: Iridodiastasis: Report of a Case with Gonioscopic Study, Chinese M. J. **69**:244-248 (May-June) 1951.

22. Blegvad, O.: Iridoschisis, Acta ophth. **29**:377-381, 1951.

23. Ashton, N., and Sorsby, A.: Fundus Dystrophy with Unusual Features, Brit. J. Ophth. **35**:751-764 (Dec.) 1951.

24. Streiff, E. B., and Portmann, U P.: Familial Occurrence of Angioid Streaks of Retina: Heredity and Pathogenesis, Ophthalmologica **121**:87-91 (Feb.-March) 1951.

25. Adelung, J. C.: Genesis of Angioid Streaks (Knapp), Klin. Monatsbl. Augenh. **119**:241-250, 1951.

Tuberculosis.—Bunn and Drobeck [26] studied the development of localized tuberculous lesions in the rabbit eye by standardizing the strain, dose, and animal characteristics. They produced nonimmunized and immunized groups of animals and found no difference in the lesions in the two groups after inoculation. The lesions could be classified under two types, the advanced, permanently destructive, and the minimal, reversible lesions. The character of the ocular lesion varied according to the size of the inoculum. Adair, Drobeck, and Bunn [27] later studied the effect of certain antituberculous agents upon these standardized ocular lesions. They found that if streptomycin and dihydrostreptomycin were given 24 hours prior to inoculation of tubercle bacilli into the eye the ocular lesions were considerably modified. When the same treatment was instituted 24 to 96 hours later, it failed to alter the course of the tuberculous lesion completely, although a major effect in slowing the disease and reducing its intensity was noted. Other agents, such as TB6 (diethanol amine salt of benzaldehyde-thiosemicarbazone-4-carboxylic acid), thiazolsulfone (promizole®), paraaminosalicylic acid, oxytetracycline ("terramycin"), and BL92 (an antihistaminic agent), failed to produce a comparable effect. When treatment was delayed until well-established ocular tuberculous lesions were present, none of the agents studied affected the disease significantly.

Belz and associates [28] describe the results obtained with the Middlebrook-Dubos hemagglutination reaction in cases of ocular tuberculosis. On the basis of 120 cases studied it was concluded that the reaction has a degree of specificity, since it was found to be positive in approximately 70% of cases of frank ocular tuberculosis. This test consists of the demonstration in the sera of persons infected with Mycobacterium tuberculosis of antibodies which specifically agglutinate erythrocytes on which an antigen obtained from Myco. tuberculosis has been fixed. These authors used a slightly modified technique, using Group-O human erythrocytes instead of sheep erythrocytes. The results were practically the same in the two instances. A positive titer is of the order of 1 : 8 or 1 : 16. Witmer [29] showed that the hemagglutination reaction is a specific antigen-antibody reaction and that the antibody is a gamma globulin. He showed that a negative hemagglutination test may become positive after a positive reaction to a tuberculin skin test. He found that control examinations showed high titers of positive agglutinins, with only two exceptions: in one case of miliary tuberculosis in an advanced stage, and in one case of Addison's disease in which the patient was in very poor general condition. Patients with sarcoidosis and scleritis often showed a high titer. This test was also made using aqueous humor, and the reaction was demonstrable in suspected cases.

The Kapuscinski test is used for the differentiation of tuberculous uveitis from uveitis due to focal infection. Typhoid vaccine, 0.01 cc., is injected intravenously;

26. Bunn, P. A., and Drobeck, B.: Use of Rabbit Eye as a Tissue to Study Tuberculosis: I. Development of Localized Ocular Lesion, Am. Rev. Tuberc. **64**:197-206 (Aug.) 1951.

27. Adair, C. V.; Drobeck, B., and Bunn, P. A.: Use of Rabbit Eye as a Tissue to Study Tuberculosis: II. Effect of Certain Antituberculous Agents upon Ocular Tuberculosis, Am. Rev. Tuberc. **64**:207-217 (Aug.) 1951.

28. Belz, A.; Sohier, R.; Bouchel, J., and Juillard, J.: Middlebrook-Dubos Type of Hemagglutination Reaction in Ocular Tuberculosis, Ann. ocul. **184**:586-605, 1951.

29. Witmer, R.: Experience with the Middlebrook-Dubos Serological Test in Tuberculosis, Ophthalmologica **123**:329-334 (April-May) 1952.

in tuberculosis there are an increase in the uveitis and an irritation of the primary tuberculous focus. In focal infection the local inflammation is reduced. Kapuscinski and Drozdowska [30] report the effect of this test with typhoid vaccine on the Mantoux reaction. They found that this nonspecific shock test caused an increase in the inflammatory signs in the skin in possible cases of tuberculosis.

Naróg [31] studied 200 cases of tuberculous meningitis for evidence of ocular lesions. Numerous fundus changes were seen in 41 of 170 cases, consisting of miliary tubercles in most instances. Damel [32] described a case of perforating tuberculoma of the choroid from which organisms were recovered.

Gandolfi and Morpurgo [33] found that thiosemicarbazone was ineffective in tuberculous disease of the retina but was partially effective in other forms of ocular tuberculosis. Lepri and Capalbi [34] found that streptomycin inhibited the development of tuberculous lesions in nonimmunized rabbits after inoculation of live tubercle bacilli. In animals treated with oxytetracycline the initial course was less severe than that in the untreated animals. After cessation of treatment the lesions became as severe as in the control series. In animals treated with oxytetracycline and streptomycin the course was similar to that observed in animals treated with streptomycin alone. The authors concluded that oxytetracycline has some antituberculous activity. Pelkonen [35] treated 42 patients with tuberculous ocular disease with streptomycin and thiazolsulfone. The diagnosis was based on the chronicity, clinical picture, and examination of the patient. One gram of streptomycin was given each day to the 42 patients. An oral dose of 6 gm. of thiazolsulfone was given to 60 other patients each day, for a total of 30 to 45 days. The results in the two groups were approximately similar. In three to four weeks the precipitates had become small, pigmented, and decreased in number. Only a weak flare and a few cells were present in the anterior chamber. In patients with choroiditis the foci became circumscribed and pigmented during treatment. It was considered that streptomycin shortens the duration of the disease, though not curing the entire process. Relapses after therapy were apt to be severe. Wegner and Zintz [36] surveyed the results obtained at a sanatorium in the modern chemotherapy of ocular tuberculosis. The data were obtained from the severest cases, in which clinical findings were strongly suggestive of a tuberculous infection of the eyes. Severe

30. Kapuscinski, W. J., Jr., and Drozdowska, S.: Diagnostic Value of the Mantoux Test in Cases of Inflammation of the Mesenchymal Tissue of the Eye Treated with Typhoid Vaccine, Arch. opht. **11**:649-660, 1951.

31. Naróg, F.: Ocular Manifestations in Tuberculous Meningitis Treated with Streptomycin, Polski tygodnik lek. **6**:259-263 (Feb. 15) 1951.

32. Damel, C. S.: Two Forms of Ocular Tuberculosis: Perforating Tuberculoma of the Choroid and Primary Tuberculosis of the Conjunctiva, Arch. Soc. oftal. hispano-am. **11**:122-135 (Feb.) 1951.

33. Gandolfi, C., and Morpurgo, F.: First Clinical Results of Thiosemicarbazone (TB 1/698) in Treatment of Ocular Tuberculosis, Arch. ottal. 1951, Spec. No., pp. 293-302.

34. Lepri, G., and Capalbi, S.: Influence of Terramycin on the Course of Experimental Ocular Tuberculosis: Comparative Activity of Terramycin, Streptomycin and Both Antibiotics Combined, Brit. J. Ophth. **36**:75-80 (Feb.) 1952.

35. Pelkonen, U.: On the Administration of Streptomycin and Promizole in Ophthalmic Diseases, Acta ophth. **30**:7, 1952.

36. Wegner, W., and Zintz, R.: Chemotherapy in Tuberculous Affections of the Eye: Preliminary Results, Klin. Monatsbl. Augenh. **119**:350-365, 1951.

pulmonary tuberculosis was present in 10% of cases; unmistakable tuberculous foci were present elsewhere in the body in 60%, and concomitant mild rheumatic symptoms existed in 13% of the 300 cases examined. Iridocyclitis was observed in 50%, uveitis in 20%, retinal periphlebitis in 20%, and choroiditis in 10% of the cases. Final conclusions were based on 103 selected cases in which amithiozone ("conteben") in daily doses of at least 0.1 to 0.15 gm. (total dose, 15 to 97 gm.) or paraaminosalicylic acid in daily doses of 10 to 15 gm. (total dose, 1,500 to 3,200 gm.) was given. Combined treatment consisted of 0.1 gm. of amithiozone and 10 gm. of paraaminosalicylic acid daily for at least five months. In only 12 cases did improvement occur within two months. In the other cases relapses were frequently observed during treatment. More rapid recovery from relapses was not observed, and the results corresponded with those previously obtained prior to the advent of chemotherapy. Prolonged treatment for approximately a year was entirely without effect in 32 cases. Improvement was observed in only 10%; no change was noted in 54%, and treatment failed in 36%. The authors concluded that ocular tuberculosis shows a much less favorable reaction to amithiozone than does tuberculosis of the lungs and other organs. A similar response was observed to paraaminosalicylic acid.

Bunn and Drobeck [37] studied the effect of adrenal cortex hormones on experimental ocular tuberculosis in the rabbit. They found that corticotropin in a dose which assures maximal response of the adrenal glands of rabbits alters the course of an ocular infection with human tubercle bacilli. The effect upon early ocular tuberculosis was deleterious. After the disease was established, the local effect was less demonstrable. Cortisone, in a probable effective dose, did not alter to the same degree the course of ocular tuberculosis in the experimental infections. Woods and Wood [38] found in the normal, nonimmune rabbit, that cortisone, corticotropin, and hydrocortisone (Compound F) have no effect in the control of inflammation or the development of tuberculous lesions. They found that topically or parenterally administered cortisone and parenterally injected corticotropin will block the focal reaction to tuberculin in the inoculum in the immune-allergic rabbit. The early development of tuberculous lesions was also blocked. Hydrocortisone appeared to be less effective than either cortisone or corticotropin in suppressing the focal reaction to tuberculin in the inoculum. After the administration of cortisone or hydrocortisone was terminated in immune-allergic rabbits, a violent increase in the degree of ocular inflammation occurred, with the development of acute and spreading tuberculous lesions in the eye—the rebound phenomenon. The rebound phenomenon probably depends on multiplication of the bacilli to the point that all immunity is overwhelmed, and thereafter the tuberculous disease assumes the destructive, necrotizing, and caseating character of tuberculosis in the nonimmune animal.

37. Bunn, P., and Drobeck, B.: Use of Rabbit Eye as a Tissue to Study Tuberculosis: III. Effect of Adrenal Hormones upon Course of Disease and upon Certain Immunologic Responses, Am. Rev. Tuberc. **66**:175-187 (Aug.) 1952.

38. Woods, A. C., and Wood, R. M.: Studies in Experimental Ocular Tuberculosis: XVI. Effect of Corticotropin, Cortisone, and Compound F on Development of Experimental Ocular Tuberculosis in Immune-Allergic and Normal Rabbit, A. M. A. Arch. Ophth. **47**:477-512 (April) 1952.

Sarcoidosis.—Jaques [39] reviewed the subject of sarcoidosis, with emphasis on the etiology and pathology of the disease. He stressed that cases of sarcoidosis can be divided into two main types—those of generalized sarcoidosis and those of focal sarcoid lesions. Focal lesions are found post mortem and in surgical specimens and are particularly prevalent in the hilum of the lung and in lymph nodes. The etiologic factor in these sarcoid lesions is obscure, but the author believes that a hyperergic response of the tissues, provoked by an unidentified agent, may be responsible. It is postulated that a nematode infection may be responsible in some cases of sarcoidosis, since they are similar in epidemiology, laboratory findings, organs involved, and histologic reactions. Longcope and Freiman [40] published an outstanding monograph on this subject, based on an investigation of 160 cases, including 30 autopsies from the Johns Hopkins Hospital and the Massachusetts General Hospital. This monograph indicated that the etiology of sarcoidosis is obscure and that demonstration of its presence depends on the histologic character of the lesions. Berman [41] reports the interesting case of a woman with sarcoidosis who had both subjective and objective improvement in the condition during two pregnancies. During the remissions the spleen returned to normal size and the albumin-globulin ratio became normal. There was no change in the pulmonary infiltration.

Ozazewski and Bennett [42] report three instances of ocular sarcoidosis. Two of the patients were treated with corticotropin; the results in the first patient were inconclusive, possibly because therapy was insufficient. The other patient showed striking subjective and objective improvement. Laval [43] presents an unusual case in which a trephination was done originally for what seemed to be chronic simple glaucoma. Two months later an iris-inclusion operation was performed, after which the eye continued to be constantly irritated. Six months later the eye had light perception only, and there were many fine cells in the anterior chamber. The fellow eye was normal. The affected eye was enucleated, and microscopic examination showed a small nodule of epithelioid cells in the nerve fiber layer of the retina. Farther posteriorly another such nodule was seen in the inner layers of the retina. There was pronounced peripapillary inflammation of the choroid and retina. A large nodule of epithelioid cells and lymphocytes lay in the nerve head adjacent to the beginning of the outer nuclear layer of the retina. The inferior portion of the globe showed similar nodules of epithelioid cells breaking through the lamina vitrea and pigment epithelium to invade the outer retina. One and one-half years later the fellow eye showed exudative choroidal lesions in the temporal periphery of the fundus. Clinical examination revealed no other evidence of sarcoidosis. Microscopic sections of this eye were examined by Dr. F. H. Verhoeff and Dr. A. B. Reese; both considered tuberculosis the most likely diagnosis, but

39. Jaques, W. E.: Sarcoidosis: Review and Proposed Etiological Concept, A. M. A. Arch. Path. **53**:558-592 (June) 1952.

40. Longcope, W. T., and Freiman, D. G.: Study of Sarcoidosis, Based on Combined Investigation of 160 Cases, Including 30 Autopsies from The Johns Hopkins Hospital and Massachusetts General Hospital, Medicine **31**:1-132 (Feb.) 1952.

41. Berman, R. H.: Sarcoidosis Benefited by Pregnancy: Report of a Case, J. A. M. A. **147**:246-248 (Sept. 15) 1951.

42. Ozazewski, J. C., and Bennett, V.: Ocular Sarcoidosis, Am. J. Ophth. **35**:547-550 (April) 1952.

43. Laval, J.: Ocular Sarcoidosis, Am. J. Ophth. **35**:551-554 (April) 1952.

they could not rule out sarcoidosis. Dr. Paul Klemperer, of the department of pathology, Mount Sinai Hospital, New York, was certain the slide showed characteristic changes of sarcoidosis.

Hedges and Taylor [44] report a case of proved Boeck's sarcoid in which the uveal tract and the vestibuloauditory system were involved simultaneously. The presenting signs suggested Harada's disease. The patient exhibited deafness, tinnitis, vertigo, and bilateral uveitis. Complete loss of vestibular function was observed on the left side 10 months after the onset. The ocular inflammation continued to be active one year after onset of the disease.

Siltzbach [45] treated 13 patients with sarcoidosis by administration of cortisone. Cortisone appeared to exert a suppressive effect upon the lesions. The author summarized the literature on this subject and noted that 23 patients with sarcoidosis showed objective and subjective improvement of varying degree while under the influence of corticotropin or cortisone. The lesions tended to relapse promptly on withdrawal of the drugs. Of the author's patients with severe disability, five obtained relief from their major symptoms during therapy, and in no patient could progression of lesions be detected during treatment. Seven of 10 patients showed a relapse after cessation of therapy. Thirteen post-treatment biopsy specimens from eight patients were available for comparison with specimens removed prior to treatment. Ten of these showed slight to advanced regressive changes.

Brucellosis.—Kuzherskaya [46] investigated 101 patients having established brucellosis and found only 1 patient with iridocyclitis. Two additional patients showed bilateral optic atrophy and bilateral optic neuritis. Pagliarani [47] found the optic nerve to be most commonly affected in brucellosis, and the uvea and retina were less often involved. He describes a case of probable arachnoiditis with secondary involvement of the optic nerve. This case is similar to one reported by Puig Solanes at the Pan-American Congress of Ophthalmology, México, D. F., in January, 1952. In a subsequent article,[48] this author describes four cases of arachnoiditis accompanied by optic neuritis, uveitis, and bilateral dacryoadenitis. Swan and associates [49] describe an acute case of brucellosis in a packing-house worker who acquired the disease from handling infected carcasses. Unilateral acute choroiditis was observed. The disease responded to treatment with streptomycin and sulfadiazine.

Sympathetic Ophthalmia.—Scheffler [50] published the findings in a case of sympathetic ophthalmia which developed 2½ months after a cataract extraction compli-

44. Hedges, T. R., and Taylor, G. W.: Uveal and Vestibuloauditory Disease with Sarcoid, A. M. A. Arch. Ophth. **48**:88-89 (July) 1952.

45. Siltzbach, L. E.: Effects of Cortisone in Sarcoidosis: Study of 13 Patients, Am. J. Med. **12**:139-160 (Feb.) 1952.

46. Kuzherskaya, A. V.: Involvement of the Anterior Segment of the Eye and of the Visual Acuity in Brucellosis, Vestnik oftal. **30**:10 (Jan.) 1951.

47. Pagliarani, N.: Contribution to the Knowledge of Ocular Manifestations Due to Brucella Infection in Man, Ophthalmologica **122**:32-45 (Jan.) 1951.

48. Pagliarani, N.: Brucella Infection in Man, Ophthalmologica **122**:31-45 (July) 1951.

49. Swan, M. M.; McClellan, J. W., and Reizman, B.: Choroidal Lesion in Acute Brucellosis Which Responded to Streptomycin and Sulfadiazine, A. M. A. Arch. Int. Med. **88**:258-261 (Aug.) 1951.

50. Scheffler, M. M.: Sympathetic Ophthalmia, Following Purulent Endophthalmitis (Post-cataract Extraction), Am. J. Ophth. **34**:1427-1430 (Oct.) 1951.

cated by purulent endophthalmitis and phthisis bulbi. Simmonds [51] performed an iridotasis on a blind eye with secondary glaucoma due to an old injury. Approximately 1½ months after operation the fellow eye showed signs of irritation and the glaucomatous eye was enucleated. Microscopic examination showed sympathetic uveal inflammation. The good eye finally recovered 20/20 vision after prolonged severe inflammation. Di Luca [52] studied 27 cases of this disease. In nine cases it developed after a surgical procedure. In eight of the nine cases the condition occurred after cataract extraction, and in one, after iridectomy. In two other cases it appeared after evisceration of the eye, and to the author this suggested that enucleation is preferable to evisceration.

Vesterdal [53] treated six patients having sympathetic ophthalmia with corticotropin. All showed rapid initial improvement. Three patients recovered completely, and in two of them the exciting eye was enucleated prior to institution of therapy. In one the remission was partial, and symptoms recurred upon withdrawal of the drug.

Haik and associates [54] observed a discrepancy between the clinical and the histologic findings in a sympathizing eye which was removed after a cataract extraction. In a review of the literature on this subject, they found a disproportionately greater infiltration of the anterior than of the posterior uvea, predominance of plasma-, mononuclear-, and polymorphonuclear-cell infiltration of the vitreous, and occasional gliosis of the inner portion of the retina. As a result of these observations, the authors suggest that a bilateral form of endophthalmitis phacoanaphylactica has apparently been confused clinically with sympathetic ophthalmia. Eighty cases of sympathetic ophthalmia were collected from the records of various ophthalmologists, from the literature, and from the authors' personal experience. Seventy-two of these reports were considered to afford sufficient data for study. In 29 cases there was a good response to cortisone or corticotropin therapy; in 18, a good response with relapse following therapy, and in 25, a poor response. Of the cases in which treatment was given early, a good response was obtained in 19, a good response followed by relapse on cessation of treatment, in 17, and a poor response, in 12. These results suggest that corticotropin and cortisone are more effective if given early in the course of the disease, and in sufficient dosage. They are also more likely to be effective in mild than in severe sympathetic ophthalmia.

Uveitis Associated with Cutaneous and Meningeal signs.—Benedict and Benedict [55] report the occurrence of this syndrome in siblings. They refer to the only previous report, that of Salus, in which the disease occurred in two sisters. In the present report the disease appeared in the two members of the family at an interval

51. Simmonds, N. T.: Sympathetic Ophthalmia Following Iridotasis: Report of a Case, Am. J. Ophth. **34**:1601-1602 (Nov.) 1951.

52. di Luca, G.: Sympathetic Ophthalmia from Clinical and Therapeutic Point of View, with Special Reference to Roentgen Therapy, Boll. ocul. **30**:354-384 (June) 1951.

53. Vesterdal, E.: ACTH in the Treatment of Sympathetic Ophthalmia, Acta ophth. **29**:239-254, 1951.

54. Haik, G. M.; Waugh, R. L. Jr., and Lyda, W.: Sympathetic Ophthalmia: Similarity to Bilateral Endophthalmitis Phacoanaphylactica, A. M. A. Arch. Ophth. **47**:437-453 (April) 1952.

55. Benedict, W. H., and Benedict, W. L.: Uveitis, Poliosis, and Alopecia in Siblings, A. M. A. Arch. Ophth. **46**:510-512 (Nov.) 1951.

of two months. The first patient was a girl, aged 17, who had severe bilateral diffuse uveitis. Three months later almost complete alopecia occurred. Nine months later the hair commenced to grow back, but was white, and the eyelashes turned white. Vitiligo and hearing defects were not noted. After a considerable period, and several surgical procedures, vision was lost in both eyes. In the brother, aged 19, there developed severe anterior uveitis, alopecia of a partial type, and vitiligo of the hair and lashes. After several surgical procedures useful vision was obtained in each eye. Flynn [56] recorded the case of a Negro woman aged 34 who had uveitis in the right eye in 1944. A complicated cataract was observed in 1945. After 1947 progressive vitiligo of the body, neck, and upper extremities developed. Some poliosis developed in the hairs about the posterior neck region. In 1949 uveitis occurred in the left eye. A paternal aunt and the paternal grandfather also had vitiligo. Contrary to the general opinion that lymphocytic meningitis is seldom to be found in patients with chronic uveitis, with the exception of the Vogt-Koyanagi and Harada syndromes, Hallermann [57] found it occurring in 22 of 41 cases after a systematic examination of the cerebrospinal fluid.

Uveitis Associated with Joint Disease.—It is well known that inflammatory and degenerative lesions are present in the skeletal muscles of patients with rheumatoid arthritis. Norcross and associates [58] studied muscle biopsy specimens and rheumatoid nodules from 18 of 30 patients prior to treatment with cortisone and corticotropin and after a satisfactory period of therapy. Only 11 patients had sufficiently significant changes in the muscles to allow evaluation of therapy. Eight of the 11 patients appeared to be definitely improved. The inflammatory rheumatoid nodules disappeared in five and were improved in eight patients.

Birbeck and associates [59] found that 13 of 148 patients with ankylosing spondylitis had associated iritis. The authors made the interesting statement that they had recently met no fewer than 11 patients with ankylosing spondylitis whose presenting symptom was iritis. The actual cause of the iritis found in this condition is conjectural. In view of the fact that radiation therapy is effective in ankylosing spondylitis, it is advisable to survey all patients with nongranulomatous iridocyclitis for evidence of spondylitis.

Hilding [60] describes a syndrome of pathologic body cartilage, destructive iridocyclitis, and multiple joint dislocations in a 61-year-old patient. The patient became blind as a result of severe destructive iridocyclitis. The articular changes differed from rheumatoid arthritis in that there was no ankylosis of the joints and little or no damage to the joint surfaces. The joint capsules were so lax that multiple dis-

56. Flynn, G. E.: Bilateral Uveitis, Poliosis, and Vitiligo: With an Hereditary Factor, Am. J. Ophth. **35**:568-572 (April) 1952.

57. Hallermann, W.: Syndrome of Uveo-Meningitis, Ophthalmologica **124**:57-58 (July) 1952.

58. Norcross, B. M.; Lockie, L. M.; Constantine, A. G.; Talbott, J. H., and Stein, R. H.: Effect of Cortone and ACTH on Histopathologic Lesions of Rheumatoid Arthritis, Ann. Int. Med. **36**:751-764 (March) 1952.

59. Birbeck, M. Q.; Buckler, W. St. J.; Mason, R. M., and Tegner, W. S.: Iritis as the Presenting Symptom in Ankylosing Spondylitis, Lancet **2**:802-803 (Nov. 3) 1951.

60. Hilding, A. C.: Syndrome of Cartilage Pathology, Destructive Iridocyclitis, Multiple Joint Dislocations: Comparison with Concurrent Eye and Joint Diseases Described in Literature, A. M. A. Arch. Ophth. **48**:420-427 (Oct.) 1952.

locations resulted. The cartilages of the nose disappeared; the ear cartilages became hypertrophic, and the rib cartilages became soft. The author points out that the syndrome in this case differed from the Ehlers-Danlos syndrome in that the patient was in an older age group and some of the other characteristics were lacking.

Relapsing Iridocyclitis with Mucocutaneous Lesions (Behcet's Disease).—This disease is relatively rare, chronic, and of unknown cause. Repeated attacks of iridocyclitis occur with increasing frequency and gradually produce irreversible loss of vision. In the later stages the attacks are accompanied by hypopyon formation. Aphthous ulcerations occur in the mucosa of the mouth and female genital tract, and ulcerations on the labia majora may be noted. France and associates[61] state that thrombophlebitis was noted in 25% of 33 cases observed. Biopsies indicated the presence of inflammatory reactions involving the small blood vessels, particularly the veins. The lesions were nonspecific. Bacteriological studies failed to reveal a causative organism. No form of treatment was found to be of value. Gilbert[62] stresses the severe, progressive character of the disease, with involvement of the synovial membranes, meninges, and liver. He maintains that the disease closely resembles "moon blindness" of horses, which is known to be due to leptospirosis. He states that he has seen two cases in which agglutination tests were positive for leptospirosis, though he does not state the specific Leptospira incriminated. In other cases the serum reaction was negative, but these observations were made late in the course of the disease. Pau[63] describes two cases in which fundus lesions, associated with other inflammatory manifestations, were presented. In the second case a hypopyon was observed. Puncture of the anterior chamber and culture of the aqueous humor yielded an anaerobic Diplococcus, which was grown in liver bouillon. A similar organism was later isolated from ulcers in the mouth. Pau thinks this organism is the same as that described by Behcet. He was uncertain whether these organisms were the true cause of the uveitis.

Rift Valley Fever.—Rift valley fever is a disease which occurs in Africa. It is caused by a virus which infects sheep and cattle, resulting in liver necrosis and death. The disease is transmissible to man, the patient having a febrile reaction, prostration, headache, and muscular pains. Persons associated with infected sheep and cattle and veterinarians or other persons who do autopsies on animals dying of the disease are susceptible to the infection. The responsible virus is possibly carried by a mosquito. During 1951 a serious animal epidemic occurred in South Africa, causing many deaths. Some humans also became infected, and a number of patients had ocular lesions. Freed[64] describes a case with a unilateral elevated macular mass, resembling central serous retinopathy. The complement fixation test was positive in a titer of 1:50. The typical clinical symptoms were present.

61. France, R.; Buchanan, R. N.; Wilson, M. W., and Sheldon, M. B. Jr.: Relapsing Iritis with Recurrent Ulcers of the Mouth and Genitalia (Behcet's syndrome), Medicine **30**:335-355 (Dec.) 1951.

62. Gilbert, W.: Ophthalmia Lenta as a Malignant Leptospirosis of the Eye, Klin. Monatsbl. Augenh. **119**:607-610, 1951.

63. Pau, H.: Clinical and Bacteriologic Findings in Ophthalmia Lenta, Klin. Monatsbl. Augenh. **119**:480-486, 1951.

64. Freed, I.: Rift Valley Fever in Man, Complicated by Retinal Changes and Loss of Vision, South African M. J. **25**:930-932 (Dec. 15) 1951.

Joubert and associates[65] describe the findings in human cases occurring in the Orange Free State, the North-Western Cape Province, and the Western and Southern Transvaal. Acute retinitis and chorioretinitis were identified as complications in a small number of cases. Approximately 50 cases of illness were encountered in farmers and their laborers. A history of intimate contact with viscera and meat was elicited in all cases. The authors state they have records of 10 cases of retinitis and chorioretinitis which occurred during the illness. Schrire[66] describes six cases of proved Rift Valley fever with ocular complications. The onset of eye symptoms after the pyrexial attack varied from two days to three weeks. The first five cases were characterized by large macular edematous areas. In the sixth case a retinal detachment occurred. The prognosis in most cases was good.

Scrub Typhus.—Scrub typhus is a mite-borne acute febrile disease caused by Rickettsia orientalis. During World War II numerous cases were observed in the Southwest Pacific and the India-Burma area. Chamberlain[67] describes a series of cases in which ocular involvement was exhibited. Two cases of rather severe bilateral iridocyclitis were observed. The changes in the iris and ciliary body developed during subsidence of the severe phase of the disease (third week). The iridocyclitis was subacute and responded slowly to treatment, pursuing a course of four to six weeks.

Lens-Induced Uveitis.—Irvine and Irvine[68] presented data characterizing the types of inflammation associated with pathologic conditions of the lens and emphasized the differentiation from a clinical standpoint of this form of inflammation from other types of uveitis. Of 128 eyes exhibiting lens injuries after trauma or operation, 12 showed inflammation of a type considered to be due to lens substance. Four additional eyes were examined in which the inflammation of the globe arose spontaneously as a result of disease of the lens. The cases were divided into groups, as follows:

1. Endophthalmitis phacoanaphylactica (nine cases). This group is characterized histologically by invasion of the lens by polymorphonuclear leucocytes and mononuclear phagocytes; the presence of giant cells and polymorphonuclear leucocytes about the lens fragments in the iris and pupillary membrane; the deposition of conglomerate precipitates on Descemet's membrane with, sometimes, proliferation of a syncytial connective tissue in the anterior chamber; cyclitic membranes, in protracted cases, and a relatively unaffected posterior segment.

2. "Phacotoxic" reactions (three cases). This group consists of cases with hypermature cataract. The lens substance, escaping into the eye cavities, produces

65. Joubert, J. D. S.; Ferguson, A. L., and Gear, J.: Rift Valley Fever in South Africa: II. Occurrence of Human Cases in the Orange Free State, the North-Western Cape Province, the Western and Southern Transvaal, South Africa M. J. **25**:890-891 (Dec. 1) 1951.

66. Schrire, L.: Macular Changes in Rift Valley Fever, South African M. J. **25**:926-930 (Dec. 15) 1951.

67. Chamberlain, W. P., Jr.: Ocular Findings in Scrub Typhus, A. M. A. Arch. Ophth. **48**:313-321 (Sept.) 1952.

68. Irvine, S. R., and Irvine, A. R. Jr.: Lens-Induced Uveitis and Glaucoma: I. Endophthalmitis Phaco-Anaphylactica, Am. J. Ophth. **35**:177-186 (Feb.) 1952; II. The "Phacotoxic" Reaction, ibid. **35**:370-375 (March) 1952; III. "Phacogenetic Glaucoma"; Lens-Induced Glaucoma; Mature or Hypermature Cataract; Open Iridocorneal Angle, ibid. **35**:489-499 (April) 1952.

uveitis and glaucoma. Pathologically, there is a pronounced plasma-cell reaction in the iris. If the lens material is exuded posteriorly, a severe cyclitis occurs, with plasma-cell and mononuclear-phagocyte response clouding the vitreous and deposition of clumps of cells on the retina and Descemet's membrane. In contrast to the picture in Group 1, giant cells and polymorphonuclear cells are relatively inconspicuous.

3. "Phacogenetic glaucoma." Clinically a consideration of this group fits best into a discussion of diseases of the lens or of glaucoma, and will not be followed further.

It is significant that of the 20 cases presented in this report, 5 were clinical cases in which the involved eye was saved by removing the lens. The authors point out that in patients with a mature or hypermature cataractous lens, the spontaneous onset of uveitis and glaucoma should lead to the suspicion that the lens is the cause. The appearance of extremely large keratic precipitates and the finding of a high protein content of the aqueous indicate the presence of lens substance in the anterior chamber. In the case of an injury or operation on one eye lens-induced iridocyclitis does not develop in the second eye unless there has been leakage of lens substance into the ocular cavities.

Müller [69] studied lens sensitization in experimental animals. He was able to show that repeated intramuscular injections of adjuvant (a compound of liquid petrolatum U. S. P., an oxycholesterol-petrolatum ointment base [aquaphor*], and killed tubercle bacilli) in rabbits may produce such a change that a subsequent discission of the lens is followed by a hyperergic reaction. He demonstrated that toxins which happen to be present in the body may cause an increased reaction to homologous lens material. Intravenous injections of toxin on the day preceding and on the day following the first discission resulted in markedly increased reactions. Twenty-three injections of cataractous lens material into the anterior chamber did not result in any convincing evidence of a "primary toxicity" of lens itself. Rabbits sensitized against heterologous, homologous, and autologous lens material in connection with intramuscular injections of adjuvant resulted in an increased hyperergic reaction in 68 of 77 eyes after a discission was performed.

Uveitis Due to Remote Infections.—Witmer [70] discusses a case of uveitis due to bronchiectasis and described the character of this form. The patient, a woman aged 67 with a subacute iritis of the left eye, formerly had an iritis of the right eye for which an iridectomy had been done, and a secondary cataract had developed. A diagnosis of bronchiectasis was made after x-ray and other examinations. After penicillin-streptomycin inhalations the bronchiectasis improved, and the uveitis was cured. Three similar cases were cited. Witmer states that the type of uveitis in patients with bronchiectasis is chronic, remittent, and similar to that observed in tuberculosis.

Uveitis Due to Higher Plant and Animal Parasites.—Leptospiral Uveitis: Alexander and associates [71] point out that in one of the four cases originally reported

69. Müller, H.: Experimental Studies on Phacogenetic Ophthalmia in Animals, von Graefes Arch. Ophth. **153**:1-35, 1952.

70. Witmer, R.: Chronic Uveitis with Bronchiectasis, Ophthalmologica **123**:352-353 (April-May) 1952.

71. Alexander, A.; Baer, A.; Fair, J. R.; Gochenour, W. S., Jr.; King, J. H., Jr., and Yager, R. H.: Leptospiral Uveitis: Report of Bacteriologically Verified Case, A. M. A. Arch. Ophth. **48**:292-297 (Sept.) 1952.

by Weil iridocyclitis developed six weeks after clinical onset of the disease. Since this time ocular lesions have been reported during or after infection with almost any of the leptospiral strains. The incidence of ocular involvement in the leptospiroses has been variously reported as from 10 to 44%. A proved case of leptospirosis occurring in one of the authors while he was working with a culture of Leptospira alexi is presented. The infection developed after accidental contamination of the left eye. The initial symptoms appeared 11 days after inoculation. Uveitis developed in the left eye 51 days after onset of the systemic illness. Cultures of the aqueous humor on the day after onset of the ocular disease yielded leptospirae on the 18th day of incubation, which were later identified as Lept. alexi. The authors were unable to demonstrate any specific effect of streptomycin or chloramphenicol and cite Hall to the effect that most antibiotics are ineffective against human leptospirosis.

Reimer [72] observed four cases of uveitis due to Leptospira during an epidemic of leptospirosis in Bremen. Otto [73] describes eight cases of benign iridocyclitis occurring late in the course of field harvest fever, which is a benign, anicteric form of leptospirosis, caused by Leptospira grippotyphosa. The iridocyclitis was a late complication and ran a chronic course. Relapses occurred in three patients, with diminished vision. In all cases the disease subsided without loss of function of the eye. Lereboullet and associates [74] reported the late development of iridocyclitis in spirochetal jaundice (Weil's disease), in spite of massive treatment with penicillin. Brauch [75] observed the occurrence of iridocyclitis five months after onset of canicola fever, possibly on the basis of allergy to the infection, as neither the blood nor the spinal fluid showed evidence of the infection.

Breese and associates [76] were unable to find morphologic difference between various Leptospira strains studied with the electron microscope. Ezell and associates [77] describe the preparation of soluble specific complement-fixing antigens for various Leptospira strains. The antigen was demonstrated in the organism-free culture liquor of each leptospiral strain studied. Haunz and Cardy [78] reported nine cases of canicola fever in one family, in North Dakota. The authors pointed out that present knowledge indicates that canicola fever is exclusively a canine infection, transmissible to man only through contact with dog excreta, chiefly the urine. Since the incidence of canicola infection in dogs may be at least as high as 38%

72. Reimer, L.: Uveitis Caused by Leptospirosis, Klin. Monatsbl. Augenh. **118**:476-482, 1951.

73. Otto, K. H.: Iridocyclitis Occurring After Harvest Fever, Klin. Monatsbl. Augenh. **120**:27-33, 1952.

74. Lereboullet, J.; Kolochine-Erber, and Lambert, P.: Hemorrhagic Nephritis Due to Leptospira, Bull. et mém. Soc. méd. hôp. Paris **67**:840-842 (June 1) 1951.

75. Brauch, F.: Iridocyclitis After Infection with Leptospira, Med. Clin. **46**:1105-1106 (Oct.) 1951.

76. Breese, S. S., Jr.: Gochenour, W. S., Jr., and Yager, R. H.: Electron Microscopy of Leptospiral Strains, Proc. Soc. Exper. Biol. & Med. **80**:185-188 (June) 1952.

77. Ezell, S. B.; Hoag, W. G.; Warner, A. R.; Yager, R. H., and Gochenour, W. S., Jr.: Soluble Specific Leptospiral Complement Fixing Antigens, Proc. Soc. Exper. Biol. & Med. **80**:220-223 (June) 1952.

78. Haunz, E. A., and Cardy, J. D.: Canicola Fever: Report of 9 Cases in 1 Family with Abstract of World Literature, A. M. A. Arch. Int. Med. **89**:978-993 (June) 1952.

(with or without active infection), it is likely that many subclinical cases in human beings escape detection. Unlike spirochetal jaundice, complications in canicola fever are infrequent and relatively mild.

Nematode Chorioretinitis: Parsons [79] reports the very unusual case of a 25-year-old white man who observed reduction of vision in the right eye. After several examinations a small subretinal worm was observed below the macula of this eye. The worm was seen to coil, uncoil, and move to various positions in the fundus. The nematode remained the same size during the three years it had been under observation. Various forms of therapy were ineffective.

Ocular Onchocerciasis: Sarkies [80] states that the severity of most manifestations of onchocerciasis increases in direct proportion to the duration of exposure. He observed living microfilariae in the anterior chamber as the commonest ocular manifestation of the disease, the number of organisms varying from hour to hour and from day to day. There was no numerical relation between microfilariae in the eye and the severity of the ocular lesions. The author states that another early ocular manifestation is macular degeneration, similar to the senile form. Disseminated chorioretinitis, isolated areas of chorioretinitis, and diffuse choriocapillary atrophy were also seen. Specific filaricidal therapy seemed not to benefit the ocular lesions observed, although the allergic side-reactions were possibly lessened. Ocular infection persisted in nearly 50% of patients three months after completion of treatment.

Toxoplasmosis.—Experimental Infections: Straub [81] studied the effect of Toxoplasma on rabbit eyes. Instillation of infected mouse ascitic fluid into the conjunctival sac produced moderately severe conjunctivitis, which proceeded to a follicular form, and then to prominent papillary hypertrophy of the mucosa. Spontaneous recovery occurred. Subconjunctival inoculation resulted in purulent keratitis and generalized infection, with death. Intraocular injection resulted in diffuse ocular inflammation. Manwell and associates [82] studied sparrows, grackles, pigeons, and gray squirrels by subinoculation of tissues and the dye test. They found that toxoplasmosis occurred only in pigeons. Some experimentally infected birds acquired a fatal infection; others, a chronic, symptomless one. The organisms underwent no change except in chickens, in which the virulence was diminished. Havlik [83] found that ticks apparently do not transmit toxoplasmosis after feeding on infected mice. Examination of infected ticks showed that Toxoplasma survives 23 days in their bodies. Fluid from excrement of infected ticks was infectious after 23 days. Blane and associates [84] found that all arthropods are readily infected, but that toxoplasmosis was apparently not transmitted by their bites. The disease could be transmitted only by inoculation of material from the infected arthropods.

79. Parsons, H. E.: Nematode Chorioretinitis: Report of Case, with Photographs of Viable Worm, A. M. A. Arch. Ophth. **47**:799-800 (June) 1952.

80. Sarkies, J. U. R.: Ocular Onchocerciasis, Brit. J. Ophth. **36**:81-99 (Feb.) 1952.

81. Straub, W.: Experimental Toxoplasma Infection in the Animal Eye, abstracted, Ophthalmologica **124**:57 (July) 1952.

82. Manwell, R. D., and Drobeck, H. P.: Mammalian Toxoplasmosis in Birds, Exper. Parasit. **1**:83-93 (Oct.) 1951.

83. Havlik, O.: Experimental Transmission of Toxoplasmosis by Ornithodoros Moubata, Časop. lék česk. **90**:1516-1518 (Dec.) 1951.

84. Blane, G.; Brunneau, J., and Chabaud, A.: Attempts to Transmit Toxoplasmosis by Arthropod Bites, Arch. Inst. Pasteur Algérie **4**:298-303, 1951.

Epidemiology: Frankhauser [85] reports eight cases of canine toxoplasmosis observed in Switzerland. Otten and associates [86] found the dye test to be positive for 49 of 122 dogs in Hamburg. Of 38 humans closely associated with 23 infected dogs, 23 had positive dye tests in titers of 1:25 to 1:400. Christiansen and Siim [87] found signs of toxoplasmosis in 264 of 2,812 wild hares examined in Denmark. Four strains of Toxoplasma were isolated from recently dead animals. Twenty-four hares gave a strongly positive dye test in titers from 1:250 to 1:6,250 and positive complement fixation tests in titers from 1:32 to 1:1,024. The pathogenicity of the hare strains of Toxoplasma corresponded to the human R. H. strain, and the two appeared to be serologically identical.

Acquired Systemic Toxoplasmosis: Franke and Horst [88] observed 11 cases of early toxoplasmosis in adults. In three of the cases Toxoplasma was demonstrated in the spinal fluid or puncture material from organs and, occasionally, in blood smears. Mouse transmission was successful once. Four patients were treated intravenously with a 20% neutral aqueous solution composed of equal parts of 2-sulfanilamido-4-methylpyrimidine (sulfamerazine) and the 3-aminobenzene sulfothiocarbamide salt of 4-aminomethylbenzenesulfonamide, 8 gm. daily for six days. Good results were obtained. Kass and associates [89] describe a case of acute toxoplasmosis in an elderly woman. The disease took the form of "spotted fever." The diagnosis was made from the histologic appearance of the lesions as seen at autopsy and in biopsy specimens of muscle. The organisms recovered were pathogenic for animals. Treatment with full courses of aureomycin, penicillin, streptomycin, sulfadiazine, corticotropin, and chloroquine was carried out, without decided effect. Serial studies on the serum for antibodies suggested that the infection was acquired. At autopsy unequivocal lesions were demonstrated only in the brain, myocardium, and striated muscle. Kabelitz [90] describes four cases of toxoplasmosis in adults with symptoms of hepatic cirrhosis and splenomegaly. Organisms resembling Toxoplasma were discovered accidentally in all four patients in sternal puncture fluid. The serologic reactions of these patients were positive for toxoplasmosis in low titer. Wollheim [91] observed 44 cases which were encountered during an epidemic of poliomyelitis. The patients had meningeal symptoms, lymphadenopathy, and splenomegaly. High titers in the dye test were found in these cases. In 14 of the patients parasites were recovered from the cerebrospinal fluid.

Siim [92] reports seven cases of acquired toxoplasmosis in young persons. Generalized lymphadenopathy was the sole finding in three cases; lymphadenopathy,

85. Frankhouser, R.: Toxoplasmosis in the Dog, Schweiz. med. Wchnschr. **81**:336-338 (April 7) 1951.

86. Otten, E.; Westphal, A., and Kajahn, E.: Epidemiology of Toxoplasmosis: The Dog as a Source of Human Infection, Klin. Wchnschr. **29**:343-346 (May 15) 1951.

87. Christiansen, M., and Siim, J. C.: Toxoplasmosis in Hares in Denmark: Serological Identity of Human and Hare Strains of Toxoplasma, Lancet **1**:1201-1203 (June 2) 1951.

88. Franke, H., and Horst, H. G.: Early Diagnosis and Treatment of Adult Toxoplasmosis, Deutsche med. Wchnschr. **76**:1049-1052 (Aug. 31) 1951.

89. Kass, E. H., and others: Toxoplasmosis in the Human Adult, A. M. A. Arch. Int. **89**:759 (May) 1952.

90. Kabelitz, H. J.: Toxoplasma Gondii in Sternal Puncture Fluid, Klin. Wchnschr. **30**:74-76 (Jan.) 1952.

91. Wollheim, E.: Clinical Aspects of Toxoplasmosis in Adults, München. med. Wchnschr. **94**:194-240 (Feb.) 1952.

92. Siim, J. C.: Acquired Toxoplasmosis: Report of 7 Cases with Strongly Positive Serologic Reactions, J. A. M. A. **147**:1641-1645 (Dec. 22) 1951.

accompanied by lassitude, fever, and nonspecific catarrhal symptoms, were noted in the four remaining cases. Strongly positive serologic reactions for toxoplasmosis were observed in all cases. Toxoplasma was not demonstrated in any of the cases. Magnusson[93] reports eight cases of acquired toxoplasmosis (two acquired in the laboratory; 5 spontaneously). The clinical picture closely resembled infectious mononucleosis. Gard and Magnusson[94] encountered a case of the disease in a woman aged 23 who presented cervical and axillary lymphadenopathy, fever, and positive serologic reactions. Pseudocysts resembling those seen in toxoplasmosis were found in an excised lymph node. The patient was pregnant, and the infant did not acquire the infection.

Congenital Toxoplasmosis: A considerable number of congenital cases were reported during the year.[95] In most cases the typical manifestations were presented in the neonatal period, or the symptoms were observed later in life, with the central nervous sequelae of this disease. Serologic studies were confirmatory in most cases, and in a number of instances parasites were recovered from the cerebrospinal fluid or tissues.

Ocular Toxoplasmosis: The most important discovery with regard to adult ocular toxoplasmosis was that of Wilder.[96] She observed organisms morphologically indistinguishable from Toxoplasma in the chorioretinal lesions in 53 eyes from the Registry of Ophthalmic Pathology, Armed Forces Institute of Pathology. The patients were from 14 to 83 years of age, and ocular symptoms were observed for from a few weeks to 32 years prior to enucleation. The patients were free from general symptoms which might indicate systemic toxoplasmosis. The lesions in which organisms were found were all alike and were characterized by focal involvement of the retina, choroid, and, frequently, the sclera. They were posterior, equatorial, or peripheral, and occasionally more than one lesion was present in a single eye. At the center of each lesion the retina was necrotic, and in the necrotic zones both extracellular and intracellular parasites were observed.

93. Magnusson, J. H.: Clinical Symptomatology of Human Toxoplasmosis, Nord. med. **45**:344-349 (Oct.) 1951.

94. Gard, S., and Magnusson, J. H.: A Glandular Form of Toxoplasmosis Associated with Pregnancy, Acta med. scandinav. **141**:59-64 (Nov.) 1951.

95. Dontenwill, W.: Toxoplasma Encephalomyelitis with Subtotal Destruction of the Cerebellum: Report of a Case, Zentralbl. allg. Path. **88**:43-46 (Nov.) 1951. Christen, R.; Agosin, M.; Pino, F.; Jarpa, A.; Thiermann, E., and Neghme, A.: First Case of Human Toxoplasmosis Confirmed in Chile, Rev. méd. Chile **79**:714-716 (Nov.) 1951. Allen, F. A.: Congenital Toxoplasmosis: A Case in Kansas, J. Kansas M. Soc. **52**:577-581 (Dec.) 1951. Rabkin, J., and Jovett, S. N.: Congenital Toxoplasmosis, South African M. J. **26**:41-43 (Jan.) 1952. Lelong, M.: LeTan Vinh, R. J., and Dupré-Bouteloup, L.: A Toxoplasmosis in the Newborn: Report of a Case, Bull. et mém. Soc. méd. Hôp. Paris **67**:541-553 (April 20) 1951. Jack, I. B.: Toxoplasmosis, M. J. Australia **1**:391-396 (March) 1952. von Sydow, G.: Acute Infantile Toxoplasmosis, Nord. med. **47**:565-567 (April) 1952. Svanborg, N. A.: Acute Infantile Toxoplasmosis, ibid. **47**:567-569 (April) 1952. Neiditsch, L.: Clinical Observations on Cases of Toxoplasmosis and Autopsy Findings in Animals and in Man, Schweiz. med. Wchnschr. **81**:485-491 (May 26) 1951. Gard, S.; Magnusson, J. H., and Hagberg, E.: Congenital Toxoplasmosis, Acta pædiat. **41**:15-31 (Jan.) 1952. Frenkel, J. K., and Friedlander, S.: Toxoplasmosis, Public Health Bull., U. S. Federal Security Agency, Public Health Service, 1951.

96. Wilder, H. C.: Toxoplasma Chorioretinitis in Adults: Preliminary Study of 41 Cases Diagnosed by Microscopic Examinations, A. M. A. Arch. Ophth. **47**:425 (April) 1952; Toxoplasma Chorioretinitis in Adults, ibid. **48**:127-136 (Aug.) 1952.

Pillat [97] describes four cases of possible ocular toxoplasmosis characterized by focal macular lesions. In his opinion the foveal lesion commences in the retina and secondarily involves the choroid. In his cases the serum gave positive results in the dye test, oftenest in low titer, and serial studies were not performed. Wising [98] observed a woman hospital employee aged 31 who presented fever, lymphadenopathy, mononucleosis, and juxtamacular chorioretinitis. The Paul-Bunnell test for infectious mononucleosis was negative. The dye and complement fixation tests for Toxoplasma gradually became strongly positive. Organisms could not be identified in the fluid from sternal punctures.

Rieger [99] reports four cases in which a central external exudative retinitis was exhibited. He considered them instances of toxoplasmosis, although the serologic titers were of a low order, and serial testing of the serum was not done. Ten similar cases [100] were later added. In this report the author studied the titers serially over a period of 10 months, and in one case the titer showed a steady rise.

Diagnosis of Toxoplasmosis: Biagi [101] studied 231 unselected persons with the skin test; 48% showed a positive response. The highest percentage (66%) of positive reactions occurred in the age group between 31 and 40. Fischer [102] made a survey with toxoplasmin skin antigen in English children. Mouse peritoneal fluid antigen was used. Positive tests were obtained in 17.5% of adults over the age of 15. The author found complete correlation between the positive reaction to toxoplasmin and the result of the dye test. The findings of Thalhammer [103] agreed with those reported above.

Straub [104] regarded a dye test titer of 1:25 as significant if the clinical findings correlate with this laboratory finding.

Westphal [105] and Steen and Kass [106] describe new methods of preparing antigen for the Toxoplasma complement fixation test. Westphal [107] seems to have shown that the sensitiveness of the dye test for toxoplasmosis depends on the type of

97. Pillat, A.: Fundus Oculi in Early Adult Toxoplasmosis, Oesterr. Ztschr. Kinderh. **6**:38-52, 1951.

98. Wising, P.: Lymphadenopathy and Chorioretinitis in Acute Adult Toxoplasmosis, Nord. med. **47**:563-565 (April) 1952.

99. Rieger, H.: Toxoplasmosis Acquired in Adult Life, Klin. Monatsbl. Augenh. **119**:459-476, 1951.

100. Rieger, H.: A Further Report on Cases of Central External Exudative Retinitis Presumably Caused by an Acquired, Adult Toxoplasmosis, Klin. Monatsbl. Augenh. **120**:33-50, 1952.

101. Biagi, F. F.: Intracutaneous Tests with Toxoplasmin at Tampico, Rev. méd. Hosp. gen. **14**:191-195, 1951.

102. Fischer, O. D.: Toxoplasma Infection in English Children: A Survey with Toxoplasmin Intradermal Antigen, Lancet **2**:904-906 (Nov. 17) 1951.

103. Thalhammer, O.: Status of Toxoplasmosis Research in Vienna, Wien klin. Wchnschr. **63**:565 (Aug. 10) 1951.

104. Straub, W.: Toxoplasmosis, with Particular Consideration of Ocular Symptomatology, Klin. Monatsbl. Augenh. **118**:66, 1951.

105. Westphal, A.: A New Toxoplasmosis Complement Fixation Reaction, Ztschr. Tropenmed. u. Parasitol **3**:191-204 (Oct.) 1951.

106. Steen, E., and Kass, E.: A New Toxoplasma Antigen for Complement Fixation Test, Acta path. et microbiol. scandinav. **28**:36-39, 1951.

107. Westphal, A.: Dependency of Titration Value in the Sabin-Feldman Test upon the Methylene Blue, Ztschr. Tropenmed. u. Parasitol. **3**:72-77 (June) 1951.

methylene blue used. Using various commercial products, he observed shifts in titer of as much as 1:32, or five tubes of the test line. The brand of methylene blue used in German laboratories yields titers averaging four times those of American workers, or two tubes lower than in the line.

NEOPLASMS

Malignant Melanoma.—A number of malignant melanomas involving the iris and ciliary body are reported.[108] Stallard[109] discusses the surgical treatment of malignant melanomas of the iris. He believes that enucleation of the eye is not justified when the tumor is confined to the iris. For excision of these tumors he makes a large flap by incising the conjunctiva at the limbus around half the circumference. An ab externo incision is made. Two iris forceps grasp the iris outside the margin of the tumor, and incisions are made outside the forceps. The wound is closed by a corneoscleral suture. The author describes the results in five cases in which the tumor was successfully removed.

Sautter and Hager[110] studied the effects of epinephrine and acetylcholine on melanoblastomas. They treated rabbit eyes with epinephrine alone or with acetylcholine in the form of drops or subconjunctival injections for periods up to 11 months. White rabbits showed no change, but in brown rabbits the epinephrine injections resulted in a brown-black discoloration, with tumor-like elevations resembling true malignant melanoma. Acetylcholine seemed to inhibit formation of these tumors. Histologic examination of the tumors showed them to have the character of true melanomas. Three patients were treated by intramuscular injections of 0.2 gm. of acetylcholine twice a day. A suppository containing 0.3 gm. of acetylcholine was given morning and evening. Every second day 0.2 to 0.3 gm. of acetylcholine was injected into the tumor. Marked regression of the tumors was observed in these cases.

Wilder[111] reported a 10-year follow-up study of 2,535 cases of malignant melanomas of the ciliary body and choroid. Of these cases, only 11 were of Negroes. The less malignant tumors were found in younger age groups (under 30). One hundred per cent of patients with the epithelioid-cell type were dead in 10 years; 78% of those with the mixed type; 70% of those with the necrotic form; 44% of those with the fascicular type; 35% of those with the spindle-cell-B type, and 20% of those with the spindle-cell-A type. Of 144 patients with extrabulbar extensions at the time of enucleation, 108 died of metastases, and epithelioid cells were found in the metastases in every case. In this series the rate of death from metastases five years after enucleation was 45%; after 10 years it was 62.2%.

108. Rockwell, P. A.: Annular Melanoma of the Iris and Ciliary Body, A. M. A. Arch. Ophth. **48**:1100 (July) 1952. Reeh, M. J.: Unusual Cases of Malignant Melanoma Involving the Iris and Ciliary Body, Tr. Pacific Coast Oto-Ophth. Soc. **32**:133-142, 1951. Hicks, J. D.: Melano-Carcinoma of the Ciliary Body, Australian & New Zealand J. Surg. **21**:153-155 (Nov.) 1951. Winter, F. C., and Maumenee, A. E.: An Unusual Pigmented Tumor of the Iris, A. M. A. Arch. Ophth. **46**:438-440 (Oct.) 1951.

109. Stallard, H. B.: Surgery of Malignant Melanoma of the Iris, Brit. J. Ophth. **35**:774-783 (Dec.) 1951.

110. Sautter, H., and Hauger, H.: Influence of the Autonomous Nervous System on the Development of Growths, Especially Melanoblastoma, von Graefes Arch. Ophth. **151**:156-166, 1950.

111. Wilder, H. C., and Paul, E. V.: Malignant Melanoma of the Choroid and Ciliary Body: A Study of 2,535 Cases, Mil. Surgeon **109**:370-378 (April) 1951.

Nadbath and Bullwinkel [112] report a case in which an intraocular melanoma developed in a patient with lymphatic leukemia. In some cases the diagnosis of intraocular malignant melanomas is frequently difficult, especially if the tumor is located posteriorly or a massive retinal separation is present. Kauffman [113] established the diagnosis by aspiration biopsy in one case. Scarney and Crossen [114] used radioactive phosphorus to aid in the diagnosis in another case. In two other cases in which an intraocular tumor was suspected, tracer studies gave negative results, and up to the time of the report there had been no clinical evidence. Thomas and associates [115] describe eight cases of suspected intraocular tumor which were studied with radioactive phosphorus. The results of these preliminary investigations suggest that this test may become important in the diagnosis of tumors. In all the cases studied the lesions were situated in the anterior choroid and were readily accessible for counting.

Reese [116] describes four cases of rather well-localized, pigmented tumors in the periphery of the iris associated with skin nevi, predominantly on the same side of the face. In two of the four cases there were freckles on the affected iris and none on the fellow iris. In two additional cases a nevus-like melanoma of the iris was associated with a nevus of the margin of the lower lid of the fellow eye. In one case a possible choroidal nevus was associated with an extensive ipsilateral pigmented nevus of the skin of the head and eyelids.

Tumors of the Iris Muscles.—Heath [117] published the findings in 19 cases of iris-muscle tumors. Sphincter tumors are compact, small, gray, or slightly yellowish, not ordinarily accompanied by pigment, and found oftenest in the lower half of the iris. Microscopically, the tumor is composed of relatively regular-sized spindle cells arranged in whorls and interlacing bundles. The muscle cells do not branch and are free from pigment. Fibrous, nonbranching myoglial elements are characteristically present. Differentiation is aided by various stains. Metastasis does not occur. In rare instances these tumors appear more malignant, as suggested by a richer blood supply, more fusiform round cells, the presence of mitotic figures, and hyperchromatic nuclei, with a more granular chromatin. Clinically, tumors of the dilator muscle appear as pigmented growths away from the pupillary zone. Growth is usually in an anterior direction and may be accompanied by proliferation of the posterior pigment layer. Tumors of the dilator are less circumscribed than tumors of the sphincter. The cells may be atypical in size, nuclear structure, fibrous cell processes, and cell arrangement. Differential stains and depigmentation of the iris are necessary to conclusive demonstration of myoglial elements. In general, tumors arising from the sphincter are more benign than those from the dilator.

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112. Nadbath, R. P., and Bullwinkel, H. G.: Coexistence of Intraocular Melanoma and Lymphatic Leukemia, A. M. A. Arch. Ophth. **48**:349-351 (Sept.) 1952.

113. Kauffman, M. L.: Aspiration Biopsy of Malignant Melanoma of Choroid, A. M. A. Arch. Ophth. **47**:541-542 (April) 1952.

114. Scarney, H. D., and Crossen, R. J.: An Interesting Case of Melanosarcoma, Kresge Eye Inst. Bull. **3**:53-54 (Nov.) 1951.

115. Thomas, C. I.; Krohmer, J. S., and Storaasli, J. P.: Detention of Intraocular Tumors with Radioactive Phosphorus: Preliminary Report with Special Reference to Differentiation of Cause of Retinal Separation, A. M. A. Arch. Ophth. **47**:276-286 (March) 1952.

116. Reese, A. B.: Association of Uveal Nevi with Skin Nevi, A. M. A. Arch. Ophth. **48**:271-275 (Sept.) 1952.

117. Heath, P.: Tumors of the Iris Muscle, Tr. Am. Ophth. Soc. **49**:147-166, 1951.

Metastatic Tumors.—Ellis and Scheie [118] report two cases of metastatic lesions of the eye from carcinoma of the breast. Remarkable regression occurred after sterilization by x-rays. Metastasis to the choroid was present in the left eye of one patient and in both eyes of the other. Jaensch [119] describes the case of a man aged 50 who had circumscribed scleritis in the right eye, followed by a retinal detachment, and secondary glaucoma. The eye was enucleated and found to have a carcinoma. The tumor was shown to have metastasized from the hilum of the left lung. Pillat [120] discusses the characteristics of metastases in the choroid from male breast cancers. Middleton [121] describes two instances of metastasis of carcinoma to the iris.

Miscellaneous Tumors.—Mings and Kundert [122] report the development of a xanthomatous tumor of the iris in a white woman aged 26. The tumor was removed by iridectomy, and microscopic examination revealed that it was a xanthoma. No other signs of xanthomatosis were present.

Weekers and Prijot [123] encountered a typical case of bilateral uveitis occurring during the course of lymphatic leukemia. Cure was obtained by means of contact x-ray therapy. Feinstein and Krause [124] report five new cases of involvement of the eyes by lymphomas. The authors feel that isolated lymphomatous disease of the eye or its adnexa must be regarded as a potentially generalized lesion, even though systemic spread may not occur for many years. X-ray therapy is advocated as the treatment of choice for localized ocular lesions.

118. Ellis, R., and Scheie, H. G.: Regression of Metastatic Lesions of Breast Carcinoma Following Sterilization, A. M. A. Arch. Ophth. **48**:118-120 (July) 1952.

119. Jaensch, P. A.: Diagnostic Difficulties in Metastatic Carcinoma of the Choroid, Klin. Monatsbl. Augenh. **120**:70-72, 1952.

120. Pillat, A.: Occurrence and Course of Metastases in the Choroid in Male Breast Cancer, Wien. klin. Wchnschr. **64**:222-224 (March) 1952.

121. Middleton, W. H.: Diagnosis of Metastatic Tumors of the Anterior Segment, Am. J. Ophth. **35**:1329-1334 (Sept.) 1952.

122. Mings, D. E., and Kundert, F. W.: Xanthoma of the Iris, Am. J. Ophth. **35**:583-584 (April) 1952.

123. Weekers, R., and Prijot, E.: Leukemic Uveitis, Ophthalmologica **122**:1-9 (July) 1951.

124. Feinstein, A. P., and Krause, A. C.: Ocular Involvement in Lymphomatous Disease, A. M. A. Arch. Ophth. **48**:328-337 (Sept.) 1952.

Society Transactions

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

George F. J. Kelly, M.D., *Chairman*

M. Luther Kauffman, M.D., *Clerk*

April 17, 1952

Raeder's Syndrome. Dr. E. Howard Bedrossian (by invitation).

A classification of sympathetic lesions as spinal, cervical, and paratrigeminal was discussed. The etiology, signs, and symptoms in five cases of Raeder's paratrigeminal syndrome were summarized. The anatomy of the sympathetic fibers was briefly reviewed, and, finally, a case of Raeder's paratrigeminal syndrome was reported. The case was of interest because complete recovery followed the removal of an abscessed upper lateral incisor tooth.

DISCUSSION

Dr. Robert H. Trueman: I should like to point out, from a purely historical standpoint, and also from the standpoint of the custom, or fallacy, of applying a person's name to a syndrome, that, although Raeder presented his paper in the *Norwegian Medical Journal* in September, 1918, Dr. Charles Frazier, of Philadelphia, in the October, 1918, issue of *The American Journal of Medical Sciences,* published an article entitled "An Operable Tumor Involving the Gasserian Ganglion," in which he described exactly the same signs and symptoms as those Raeder had described. Frazier referred to an article that Spiller had published in 1908, 10 years previously, in which the latter had reported two of Frazier's cases presenting similar signs and symptoms of the paratrigeminal syndrome in which operation was not performed.

If we are going to follow through with the custom of attaching a man's name to a medical condition, then, in all fairness, we should add Frazier's name to that of Raeder. Actually some neurological textbooks, namely, Grinker and Bucy's "Neurology" and Spiegel and Sommer's "Neurology of Eye, Ear, Nose, and Throat," do attach Frazier's name to the paratrigeminal syndrome, or, as it is sometimes called, paratrigeminal paralysis of the oculopupillary sympathetic fibers.

As for the syndrome itself, it is generally accepted by the neurologist and the neuro-ophthalmologist that it occurs relatively infrequently, but that it is of great importance in the localization of lesions of the middle cranial fossa.

There are three generally accepted etiologic factors. First, as Dr. Bedrossian stated, the syndrome is usually based on the development of an aneurysmal dilatation of the carotid artery or the actual development of an aneurysm of the carotid artery, which accounts for the interruption of the sympathetic fibers. Second, it can be produced by a meningeal tumor, as it was in the case in which Dr. Frazier operated, and, finally, by an inflammatory lesion.

Apparently, development of the paratrigeminal syndrome has its onset in the appearance of sensory disturbances in the face, beginning with pain, which is replaced by anesthesia and associated loss of the corneal reflex. This is usually followed by involvement of the carotid sympathetic fibers, miosis and ptosis. This, in turn, is followed by a disturbance in the muscles of mastication, with weakness, and later atrophy, of the masseter and temporal muscles. If the lesion continues

to enlarge, it may involve further neighborhood structures, such as the sixth, the third, or the fourth cranial nerve, and may even involve the temporal lobe or the midbrain.

Finally, in reviewing the cases previously reported, particularly those in Frazier's and Raeder's articles and in Walsh's textbook, it is interesting to note that the majority were unconfirmed surgically or at autopsy, but that the disturbance, as in Dr. Bedrossian's case, cleared spontaneously. In the cases that were confirmed, the most frequent cause was aneurysm, and the second most frequent was meningeal tumor. Even though the diagnosis cannot be confirmed, a tentative diagnosis can be made by the appearance of the paratrigeminal syndrome described above and by localization of the lesion made.

DR. I. S. TASSMAN: I do not know why this condition should be known by any particular man's name. Apparently, it is a type of Horner syndrome which has occurred as a result of sympathetic involvement, and sympathetic involvement may occur for any number of reasons. The most important feature of the condition in the present case was the Horner syndrome, with the ptosis on the affected side. As nearly as it has been possible to determine, the etiologic agent was an infected tooth, the left lateral incisor.

If that was the etiologic factor, how does one account for the involvement of the sympathetic, and also of the trigeminal, fibers on that same side. If it was not the cause, what other factor produced the so-called Raeder syndrome?

DR. E. HOWARD BEDROSSIAN: I cannot answer all Dr. Tassman's questions. I agree that this disorder should not be called Raeder's syndrome, but I gave it this name in the title because it is so referred to in the literature, and we should know what it means. Several ophthalmologists asked me if I meant Reiter's disease.

I think the paratrigeminal syndrome is important. If one keeps in mind this simple classification of sympathetic lesions as spinal, cervical, and paratrigeminal, the correct diagnosis will be made in more cases.

Meningioma of the Tuberculum Sellae. DR. FRANCIS C. GRANT.

The author stated that meningioma of the tuberculum sellae may give as few indications of its presence as any lesion with which the neurosurgeon has to deal. If this tumor is to be dealt with successfully and safely, the decision to operate must be based on two symptoms alone: a cut in the temporal field and mild optic nerve atrophy.

The results of the surgical attack on a tumor in this position were reported in a series of 27 cases. The importance of early diagnosis was stressed. The symptoms were monotonously uniform—always visual loss in one eye, slowly developing blindness in that eye, and diminution of acuity in the temporal field of the fellow eye. Eighteen patients were entirely blind, or had light perception only, in one eye when the diagnosis of tumor was finally made.

In this series of 27 cases, complete removal was accomplished in only 11. In 7 of these 11 cases the sella appeared normal in roentgenograms. In no case in this series in which the sella was sufficiently distorted to make the localization of the tumor obvious from this evidence alone was total extirpation considered safe. Partial removal was carried out in 16 cases; there were 8 fatalities.

DISCUSSION

DR. GLEN G. GIBSON: This excellent report by Dr. Grant, based on such a large number of cases, makes it one of the most important papers ever to appear on suprasellar meningioma. Dr. Grant's message is essentially that of early diagnosis and early operation, in order that the patient's sight, unnecessary damage to the patient's brain, and, in some cases, the patient's life may be saved. He has clearly stated that reliance cannot be placed on such standard indications of intracranial

tumor as increased intracranial pressure, choked disk, neurologic signs and symptoms, or roentgenographic evidence of bone involvement. Therefore the responsibility for early diagnosis is placed on proper testing and proper interpretation of the visual fields by the ophthalmologist.

Dr. Grant's finding that 66% of his patients at the time of diagnosis had a loss of visual acuity in one eye amounting to almost complete or complete loss of sight might imply that we ophthalmologists are somewhat tardy in our diagnosis of this condition. Perhaps if Dr. Grant were to look at his figures from the point of view of an ophthalmologist, he might remove from his records the cases in which loss of vision was advanced before the patient consulted the ophthalmologist, as well as the cases in which the condition was of long standing before this syndrome became well known.

Visual fields taken in the neurosurgical service at Temple University are presented.

The first was obtained in a case in which diagnosis was made early and the tumor removed successfully, as shown by the visual fields before and after operation. The visual field defect was of four months' duration. Visual acuity was reduced to 6/9 in the right eye and 6/12 in the left eye, and examination of the fundi revealed that the optic nerves were entirely normal. Therefore, in describing the fundi in this syndrome, it should be stated that in early cases the optic nerves appear normal. In cases of intermediate duration pallor of the disk develops, and optic atrophy is a late sign. The right eye shows two temporal scotomas, the beginning of temporal anopsia in this eye, and the left eye, a central scotoma and inferior altitudinal anopsia.

The next slide shows the characteristic field defect of a prechiasmal lesion. The visual field was taken with a 3/330 target, a relatively crude form of perimetry for the demonstration of this field defect. The 1/1000 isopter on the tangent screen and the color fields showed a much more advanced defect than is illustrated in the chart. The successful removal and the remarkable improvement in the central vision and visual fields are illustrated in the postoperative visual field one month after operation.

In contrast to the successful case just shown, a case is presented in which the history dates back four years and there were marked loss of vision and visual field in the left eye, with a central scotoma. The tumor was very large, and it was only partially removed; but there was no improvement in the postoperative field.

The final slide illustrates the fact that the visual field defect with this lesion is much greater in one eye than in the other. In this case there was hemianopsia, with a marked temporal defect in one eye, and the other eye showed inferior altitudinal anopsia, with vision reduced to hand movements in the superior nasal quadrant. The tumor was very large and involved the area anterior, superior, and posterior to the chiasm, as well as both optic nerves; yet there was a considerable difference in the visual fields in the two eyes. This case demonstrates that the detailed charts in textbooks illustrating the distribution of intrachiasmatic fibers as they curve forward are of not much practical value, for the lesions are so much larger than the entire chiasm. In this case the patient died after operation.

Dr. George F. J. Kelley: The term "early diagnosis" has been used extensively in this discussion, and in cases of pituitary lesions one certainly aims at an early diagnosis; yet progress of symptoms may be very slow. In one of Dr. Grant's slides the fields were measured two or three years before surgical intervention. It is very nice to say that the diagnosis should be made early, but often the patient complains of nothing but, possibly, headache, and it is only when some other symptom presents itself that one thinks of the syndrome. In Dr. Grant's cases, how rapid was development of the field defects? Was there any uniformity in rapidity in development?

DR. FRANCIS C. GRANT: Since patients with tumor of the tuberculum sellae complain primarily of symptoms which send them to an ophthalmologist for advice, my purpose in presenting this paper is self-evident. My further purpose is to suggest that, given a patient with unilateral optic nerve atrophy and a temporal-field cut for color and form, even if x-ray studies of the skull and pituitary areas are entirely noncontributory, the possibility of a tumor in this region being the cause of the clinical picture should be considered. Neither air study nor arteriography is a serious diagnostic test. If such a means is used in time, and frankly, I know of no other way in which one may make an early diagnosis, the tumor comes to the surgeon while it is still small, unentangled with adjacent carotid branches; and complete removal is relatively simple. When the optic nerve atrophy and temporal-field cut are bilateral, and when the sella is eroded, the diagnosis is easy. But the complete removal of the tumor, because of its size and because of involvement of a major carotid branch, may then be difficult and dangerous.

Physiological Factors in Refraction. DR. FRANCIS HEED ADLER.

Various physiological factors which have a bearing on the many problems of refraction were discussed.

DISCUSSION

DR. ALFRED COWAN: This is not an easy paper to discuss; in the first place, there is not enough for me to disagree with. I should like, however, to speak of a few points and mention their practical application in clinical refraction. A number of men have suggested, or believe and have written, that the brightness difference is a factor in visual acuity. Gullstrand stated, many years ago, that shades of brightness were more important in visual discrimination than absolute brightness. Hoffman, Hecht, Lythgoe, Hartridge, and others have suggested the same thing. Ludvigh, in his attempt to explain the low visual acuity in ametropia, which seems to be out of proportion to the degree of ametropia, described what he called the gradient of retinal illumination, but he was very careful to state that it is only one of the many factors that must be considered. Of course, as Dr. Adler stated, there are others such as adaptation, fixation tremor, and aberrations, that must also be considered. Ludvigh pointed this out in his paper. His explanation for ametropia (I think he means low visual acuity out of proportion to the refractive error) seems logical. He also stated that the defect of the correcting glass in ametropia is to increase the gradient of retinal illumination. He failed to mention the sharpness of the retinal image, and I like to think that the effect of the correcting lens is to sharpen the image on the retina, for the correcting lens optically places the object at the distance from the eye at which a clear retinal image can be received. Visual acuity is a very complicated function, far too complicated to be tested merely by the ability of a subject to distinguish two points as two, or, as we say, by the resolving power of the retina. Still, the only clinical means of testing the visual acuity in the office is with test cards based on this principle, and even these, as Dr. Adler points out, are faulty. But there is one test card that answers all the requirements for a test card, even the one made here, that the separation between the test objects should be such that each object can serve as an individual test object. Modesty forbids my mentioning the name. I do not know why more people do not use it. It has been available since 1928.

The illumination of test cards is important, as Dr. Adler pointed out. It should never be less than about 30 or 40 f.-c., and the surroundings in the room should be illuminated to within 20 to 50% of the illumination on the test card. But the illumination of the surroundings should never be greater than the illumination on the test card. The patient then will tire less easily and be a better subject. This, of course, eliminates all devices for projecting the test object. They should never be used either in testing the visual acuity or in doing the refraction.

Dr. Adler speaks of the increase in visual acuity with the increase in illumination regardless of the size of the pupil. There seems to be no limit. Lythgoe found that the visual acuity increased, as Dr. Adler showed, up to 1,000 f.-c. It has been found to increase up to 1,700 f.-c. This increase takes place regardless of size of the pupil, but in practice there is an associated contraction of the pupil with increase in illumination, and the contraction of the pupil is a very important factor in visual acuity. It reduces the aberrations; it increases the depth of focus; it can even make apparent changes in the refraction. Hess showed that the apparent difference in the refraction by contraction of the pupil may amount to 1.5 D., or even more.

Dr. Adler brought out the important point that the diffusion image is larger than a clear, sharp image. This means that whenever we do a subjective refraction, we should begin by instructing the patient on what we mean when we say, "Is this better? Is this worse?" When we add a lens, we should tell the patient offhand that we do not want him to consider whether the object seems larger or smaller, whether it seems closer or farther away, merely whether the addition makes the object seem clearer or less clear, whether it sharpens the outlines.

Dr. Francis Heed Adler: It looks to me as though Dr. Cowan and I were in good agreement, but I am a little discouraged. I spent a lot of time trying to define in terms of retinal physiology what we do in correcting ametropia; and when I get through, he says, "Well, I still prefer to say it sharpens the image on the retina."

News and Comment

EDITED BY DR. W. L. BENEDICT

GENERAL NEWS

Section on Ophthalmology, One Hundred Second Annual Session, American Medical Association.—The official program follows.

Tuesday Morning, June 2, 1953

CHAIRMAN'S ADDRESS
Francis Heed Adler, Philadelphia

SCLERAL RESECTION OPERATION FOR RETINAL DETACHMENT: AN EVALUATION OF RESULTS
Peter C. Kronfeld, Chicago, and Dohrmann K. Pischel, San Francisco

COMPARISON OF SCLERAL RESECTION AND SCLERAL FOLDING IN EXPERIMENTAL SHORTENING OF THE EYE
Angelos N. Dellaporta, Buffalo.

DIAGNOSTIC USE OF P^{32} IN OCULAR PATHOLOGY
Isadore J. Eisenberg, Irving H. Leopold, and David M. Sklaroff, Philadelphia

OCULAR DYSMETRIA, FLUTTER-LIKE OSCILLATIONS OF THE EYES, AND OPSOCLONUS
David G. Cogan, Boston

XEROPHTHALMIA
Daniel G. Vaughan Jr., San Jose, Calif.

DACRYOCYSTOGRAPHY: THE NORMAL LACRIMAL TRACT
Benjamin Milder, St. Louis, and Byron Demorest, St. Paul

Wednesday Morning, June 3

ADDRESS BY FOREIGN GUEST OF HONOR
Prof. A. Franceschetti, Geneva, Switzerland

UVEITIS IN CHILDREN
Phillips Thygeson, San Jose, Calif.; Michael J. Hogan, and Samuel J. Kimura, San Francisco

UVEITIS: A MILITARY PROBLEM
Major John R. Fair, M.C., U. S. A.

CLINICAL REPORT OF USE OF THREE NEW CYCLOPLEGIC DRUGS
Bernard C. Gettes, Philadelphia

VERY EARLY VASCULAR SIGNS IN RETINA IN RELATION TO ELEVATED DIASTOLIC BLOOD PRESSURE
Henry Minsky, New York

Thursday Morning, June 4

DORACAINE FOR RAPID ANESTHESIA OF THE CORNEA
Henry E. Schlegal Jr. and Kenneth C. Swan, Portland, Ore.

PRELIMINARY REPORT ON THE RIDLEY OPERATION
Warren S. Reese and Turgut N. Hamdi, Philadelphia

CONTACT LENSES IN APHAKIA
Elizabeth F. Constantine and John M. McLean, New York

Isonicotinic Acid Hydrazide in Ophthalmology
Theodore F. Schlaegel Jr. and Louis N. Hungerford, Indianapolis

Fibrin Film in Treatment of Corneal Diseases
C. William Weisser, Pittsburgh

Experiences with a Magnetic Implant for Cosmetic Improvement of the Enucleation Procedure over a Five-Year Period
Richard C. Troutman, New York

Reprints for "Annual Reports on Stress" Requested.—In 1950, the Institute of Experimental Medicine and Surgery, Montreal, Canada, initiated the publication of a series of reference volumes entitled "Annual Reports on Stress" (Acta Medical Publishers, Montreal), in which the entire current world literature (usually between 2,000 and 4,000 publications) is surveyed every year. Up to now, we have had to compile the pertinent literature partly from medical periodicals, monographs, and abstract journals and partly from reprints sent us by the authors themselves. Of all these, reprints have proved to be the best source of data which we have felt deserved prompt attention in our annual reports. Hence, in the past, we have sent out several thousand individual reprint requests to authors of whom we knew that they were currently engaged in research on stress and allied topics. Even this procedure did not give us the wide coverage which would be desirable.

It is evident that in order to insure prompt inclusion of publications in the annual reports, these surveys must develop into a cooperative effort between the authors of original papers and the reviewers. This cooperation was greatly enhanced of late by the publication of announcements, in several medical journals, encouraging investigators interested in stress research to send us their reprints for this purpose as soon as they become available.

Hans Selye, M.D.
Professor and Director of the Institute of Experimental Medicine and Surgery.

Alexander Horava, M.D.
Co-author of the "Annual Reports on Stress."

Western Hemisphere Conference of World Medical Association.—Dr. Derrick T. Vail, professor and head of the department of ophthalmology at Northwestern University Medical School, Chicago, will be guest participant in panel discussions at the First Western Hemisphere Conference of the World Medical Association at Richmond, Va., on April 24, 1953.

The sessions will provide opportunity for a discussion of current medical problems between representatives of the national medical societies of Latin America and the specialists and practitioners of the United States. Dr. Louis H. Bauer, President of the American Medical Association and secretary-general of the World Medical Association, will moderate at a general session, at which panel reports will be made. Dr. Vail will contribute a chapter on recent advances in ophthalmology to a volume commemorating the conference.

Ophthalmological Study Council Courses.—The Ophthalmological Study Council courses are given between June 22 and Sept. 5 and will be given in 1953 at Colby College, Waterville, Maine.

The Harvard Medical School Post-Graduate Courses in Ophthalmology are given from the end of September to the end of February. The address for the Ophthalmological Study Council (the Lancaster Courses) is 243 Charles St., Boston. The address for inquiries regarding postgraduate courses in ophthalmology at Harvard is 25 Shattuck Street, Boston.

Alumni Association of New York Eye and Ear Infirmary.—The Alumni Association of the New York Eye and Ear Infirmary will hold its annual scientific program from April 20 to 24. The scientific sessions in ophthalmology will be

held Monday and Tuesday; the sessions in otorhinolaryngology, on Thursday and Friday, at the New York Academy of Medicine, Room 440. Sessions will commence at 9:30 a. m. and 2 p. m. Wednesday will be left open for clinical and surgical demonstrations at the New York Eye and Ear Infirmary.

Seventeenth International Congress of Ophthalmology.—The Seventeenth International Congress of Ophthalmology will take place at the Waldorf-Astoria Hotel, in New York, Sept. 12 to 17, 1954. Dr. Bernard Samuels, New York, is president; Dr. John H. Dunnington, New York, vice-president, and Dr. William L. Benedict, Rochester, Minn., secretary-general. Dr. Derrick Vail, Chicago, is chairman of the Executive Committee. The chief topics for discussion are as follows:

Primary Glaucoma

Etiology and General Considerations.....Dr. Derrick Vail, Chicago
Medical Treatment..... Dr. E. Thiel, Frankfurt am Main, Germany
Surgical Treatment.....Dr. G. P. Sourdille, Nantes, France

Etiology of Uveitis

General Considerations.....Dr. Alan C. Woods, Baltimore
Allergic Factors.....Dr. Norman Ashton, London, England
Role of Viruses.....Dr. V. Cavara, Rome, Italy

A number of papers by authors on subjects of their own choosing will also be heard. English, French, and Spanish are the administrative languages of the Congress, but papers may be read in any language. Original papers should be sent to the Secretary-General not later than Jan. 1, 1954. As the number of papers submitted may be greater than can be accommodated, the Committee on Scientific Program reserves the right of selection.

A program of motion pictures will be a prominent feature of the Congress. The most approved techniques of diagnosis and treatment of ocular diseases will be demonstrated, as well as modern methods of audiovisual instruction by means of electronic instruments of projection, radio, and television. There will be large scientific and technical exhibits in the various assembly rooms of the hotel.

All qualified medical practitioners are eligible to attend the Congress. Persons who are not medical practitioners but who are engaged in scientific work in a field allied to ophthalmology may register as associate scientific members, and relatives and friends of members may attend as associate members. The schedule of registration fees, as determined by the International Council, is as follows: full members from North American countries, $25; from non-North-American countries, $15; associate scientific members from North American countries $10; from non-North-American countries $5; associate members from North American countries $10; from non-North-American countries $5.

The American Express Company has been appointed official travel agent for the Congress and will offer assistance in securing travel accommodations. In order to provide the greatest possible assistance in securing hotel accommodations, a special Housing Bureau has been established. Arrangements have also been made for low-cost accommodations in the residence halls of Columbia University.

Assistant Residency in Ophthalmology, Bowman Gray School of Medicine.—An assistant residency in ophthalmology will be available July 1, 1953, as a result of unexpected demands of the military. This service is a medical school service, fully approved by the American Medical Association, with very active outpatient service and busy surgical service. The usual resident's stipend and up-keep may be supplemented by participation in an active research program now under way. Training in the basic sciences or previous experience in ophthal-

mology is desirable, but not absolutely necessary. Inquiries should be addressed to Dr. Winston Roberts, Chief of Ophthalmology, Bowman Gray School of Medicine of Wake Forest College and North Carolina Baptist Hospital, Winston-Salem, N. C.

Course in Glaucoma, Brooklyn Eye and Ear Hospital.—A course in glaucoma, with particular emphasis on gonioscopy and study of the anterior angle, will be given at the Brooklyn Eye and Ear Hospital on May 4, 5, and 6, 1953. Ample opportunity for practical instruction in the use of the gonioscope lens will be given, and material from the glaucoma clinic will be utilized. One afternoon will be devoted to surgical indications for and technique of glaucoma surgery in the operating room.

On the faculty will be Dr. E. Clifford Place, Dr. Walter V. Moore, Dr. M. A. Lasky, Dr. Daniel Kravitz, and Dr. Arthur Shainhouse.

Application and the fee of $40 for registration of ophthalmologists may be addressed to Dr. Daniel Kravitz, Brooklyn Eye and Ear Hospital, 29 Greene Ave., Brooklyn 38.

American Association of Orthoptic Technicians.—The American Association of Orthoptic Technicians wishes to announce that a confidential placement service has been organized for positions for certified orthoptic technicians. Information regarding available technicians and positions open can be received by writing Mrs. Louisa Wells Kramer, 1779 Massachusetts Ave. N.W., Washington 6, D. C.

Charlotte Ophthalmological Society Established.—On Nov. 24, 1952, the Charlotte Ophthalmological Society was formed by the following eye physicians: C. B. Foster, W. R. Graham, T. D. Ghent, H. T. Holden, M. J. Hough, Ruth Leonard, M. J. Lymberis, H. C. Neblett, F. C. Smith, and J. D. Stratton. The officers elected were Dr. H. C. Neblett, president; Dr. J. D. Stratton, vice-president, and T. D. Ghent, secretary and treasurer. Meetings will be held bimonthly and will be of a scientific nature.

American Orthoptic Council Examination of Technicians.—The annual examination of orthoptic technicians by the American Orthoptic Council will be conducted in August and October, 1953.

The written examination will be nonassembled and will take place on Thursday, Aug. 27, in certain designated cities and officies and will be proctored by designated ophthalmologists.

The oral and practical examinations will be on Saturday, Oct. 10, in Chicago, just preceding the meeting of the American Academy of Ophthalmology and Otolaryngology.

Application for examination will be received by the office of the secretary of the American Orthoptic Council, Dr. Frank D. Costenbader, 1605 22d St. N.W., Washington 8, D. C., and must be accompanied by the examination fee of $30. Applications will not be accepted after July 1, 1953.

Books

Office Management of Ocular Diseases. By W. F. Hughes Jr., M.D. Price, $9. Pp. 452, with 120 illustrations. The Year Book Publishers, Inc., 200 E. Ill. St., Chicago 11. 1953.

This book is a timely contribution to modern ophthalmological literature. In a small volume, the author has incorporated not only a highly practical outline of therapy but also some of the most important points of diagnosis that one is apt to encounter in everyday ophthalmological practice.

The presentation of the various phases of ophthalmological office routine is clear and concise, and yet leaves out no essential details. The author manages to accomplish this in part by omitting many of the older classifications and subheadings, which have become obsolete in modern ophthalmological concepts.

His chapters on vision and optics are clearly presented, and his description of the practice of refraction brings out many practical hints, which obviously have arisen from an extensive clinical experience. The author goes into great detail on such subjects as the exact detail of evaluating visual acuity in a patient. Many small, but highly significant, points are made which would ordinarily take the young ophthalmologist several years to realize as being extremely important. Very few textbooks bring them out as clearly as does this one.

The orbit is covered rather thoroughly, for a small textbook; the chapter on the cornea is short and leaves out many of the older classifications, which are not of much value today.

The schematic sketches of some of the operative procedures, especially the office procedures, are very clear and useful. On the other hand, the black-and-white reproductions of corneal conditions are a little difficult to appreciate and would undoubtedly have been much better in color.

The chapter on uveitis is very thorough and leaves out very little detail, despite the small size of the volume. Furthermore, it brings the reader up-to-date on the concepts of modern steroid therapy. Glaucoma is handled adequately, and this section contains many practical suggestions, both in the recognition and in the treatment of this very important disease.

The chapter on retinopathies is rather short but, again, includes the most significant and practical conditions with which one should be acquainted. Again, all the fundus conditions are reproduced in black and white from actual photographs; consequently, much of the detail is rather poor. The value of this excellent little volume would have been considerably enhanced if these conditions had been represented in color.

The chapter on ocular injuries is particularly good in that it covers all possible types in a systematic manner and gives a concise description of the recognition and treatment of all of them, short of the actual operative procedures.

Radiation treatment is handled adequately, and the use of beta rays, particularly, is stressed. The amount of attention paid to radiation therapy seems a little out of proportion in a volume of this size but may be in keeping with the future of radiotherapy in ophthalmology.

While the author presents most of the prevailing points of view on various controversial subjects, he also gives some very definite ideas as to his own concepts on these subjects.

Finally, the chapter on the ophthalmic formulary brings one up-to-date on all the modern concepts of hydrogen ion concentration, tonicity, stability, and sterility of ophthalmic preparations. This chapter is followed by a complete

tabular listing of all the drugs used in ophthalmology, with detailed descriptions of the concentration and dosage of each. In keeping with the rest of this textbook, some obsolete drugs that have long been discarded by most ophthalmologists are not mentioned; instead, many of the newer drugs that have become important in everyday practice, but have not yet found their way into other textbooks, are presented in detail.

This volume is an excellent addition to any medical library. While it is an excellent source of ready information for the young ophthalmologist and the general medical practitioner, it is useful also to the busy, and even experienced, ophthalmologist, who may want a source of readily accessible information on some phases of eye diseases that he may not encounter frequently.

A Further Study of Visual Perception. By M. D. Vernon. Price, $7. Pp. 289, with 30 figures. Cambridge University Press, 51 Madison Ave., New York 10, 1952.

The author collected the chief psychological experiments on visual perception and published these in 1937. At that time the Gestalt theory held the stage. Since then, the Gestalt psychologists have turned to theoretical speculations as to the physical basis of the perceptual processes in the cerebral cortex. This book is a reassessment of the previous material in the light of more recent thought and experiment.

The book starts with a statement of the nature of perception and an outline of its development in children. The author considers spatial perception and, finally, the perception of movement from the psychological point of view.

It will be of value only to those who have training in, and a specific liking for, the psychological approach to vision.

Clinical Allergy. By French K. Hansel, M.D., M.S., Director, Hansel Foundation for Education and Research in Allergy; Chief of Allergy Service, DePaul Hospital, St. Louis. Price, $17.50. Pp. 1005, with 86 illustrations and 3 color plates. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1953.

"Clinical Allergy" is a complete text which replaces a previous, more limited presentation, entitled "Allergy of the Nose and Paranasal Sinuses," published in 1936. This new volume embraces the entire field of allergy, but still with particular emphasis on the nose, the paranasal sinuses, the ears, the eyes, and the tracheobronchial tree. With regard to the eyes, there is a special chapter, entitled "Allergy in Ophthalmology." The subjects covered in this field include diagnostic procedures, dermatologic conditions related to the eye, allergic conjunctivitis and blepharitis, vernal conjunctivitis, phlyctenular keratoconjunctivitis, keratitis, focal infection and bacterial allergy, the uveal tract, the lens, the retina and choroid, the optic nerve, and cortisone (cortone®) in the treatment of ocular conditions. An adequate bibliography is placed at the end of each chapter.

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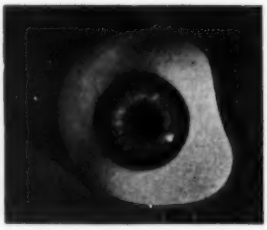

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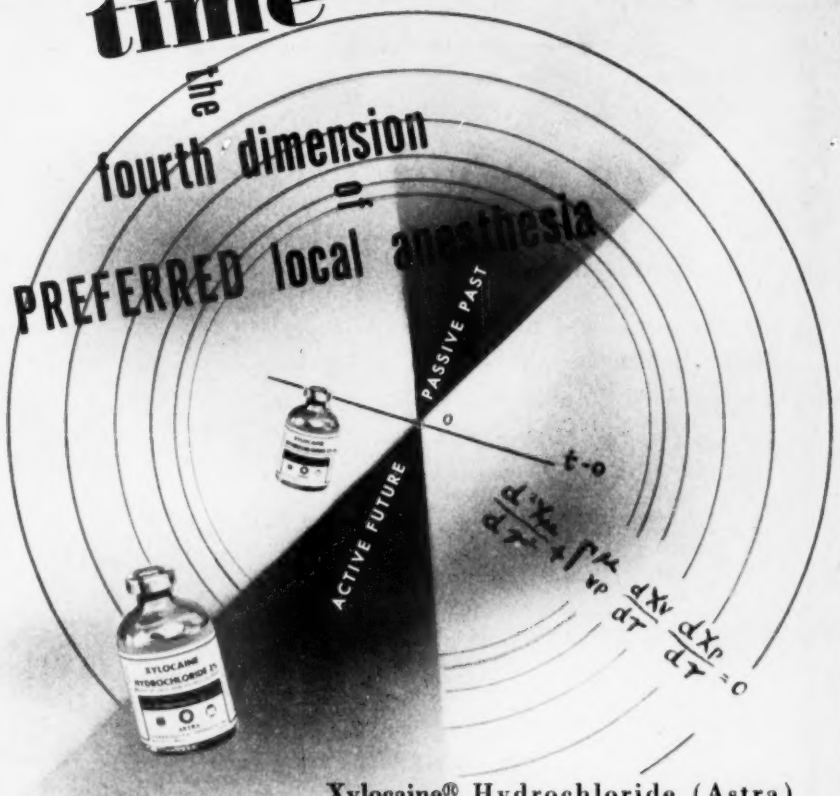

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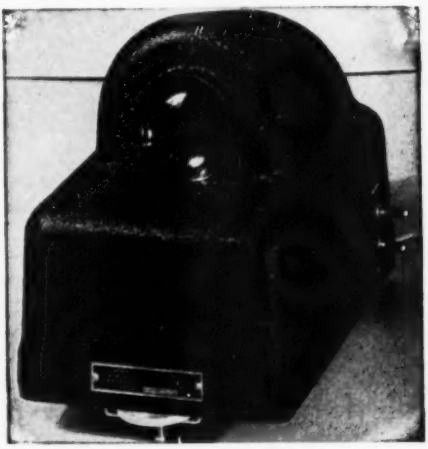

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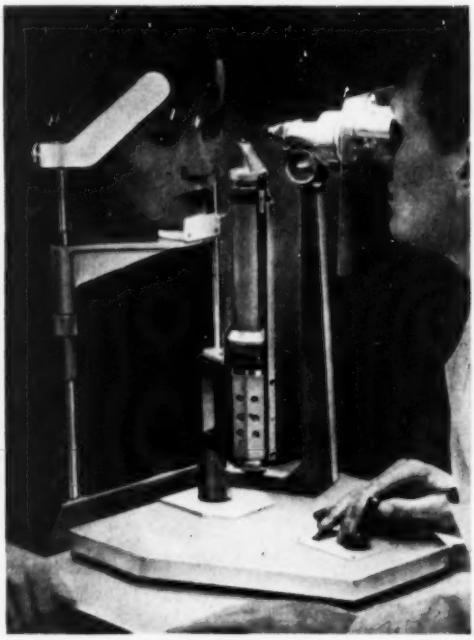

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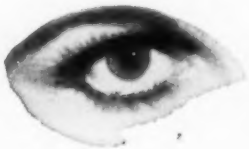

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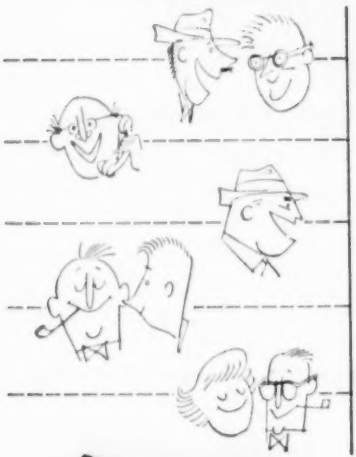

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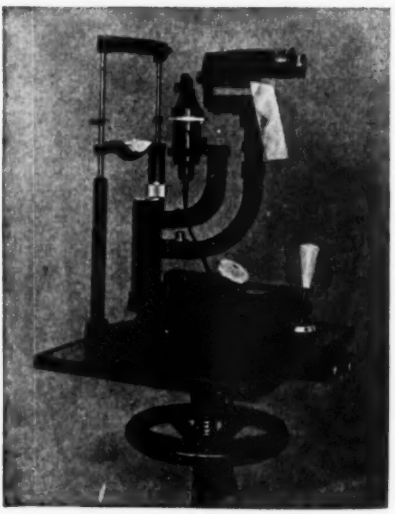

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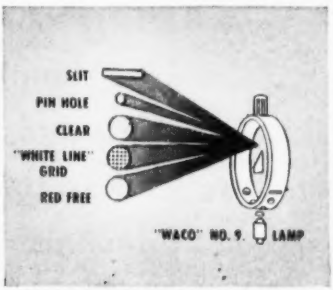

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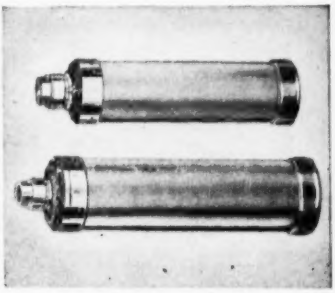

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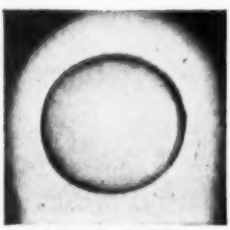

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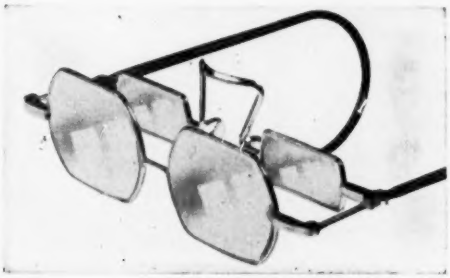

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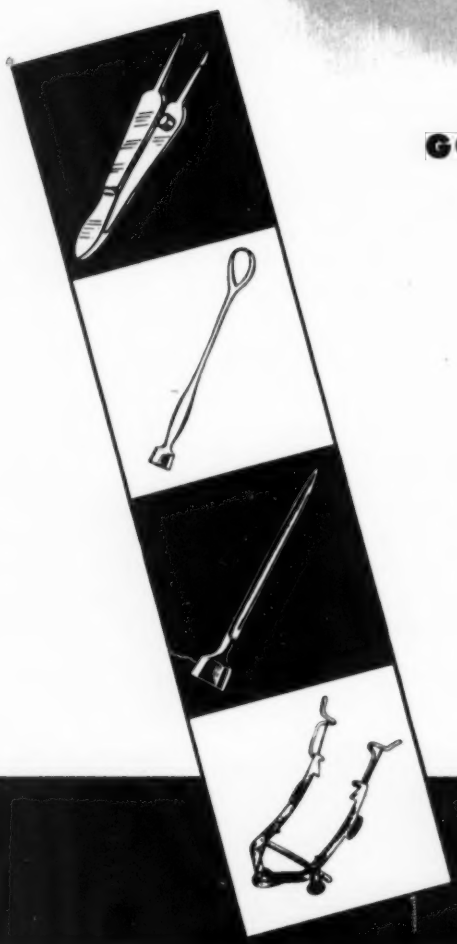

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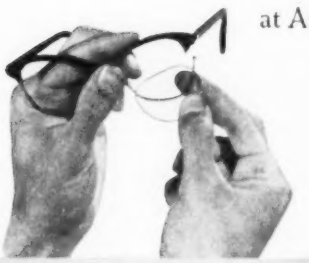

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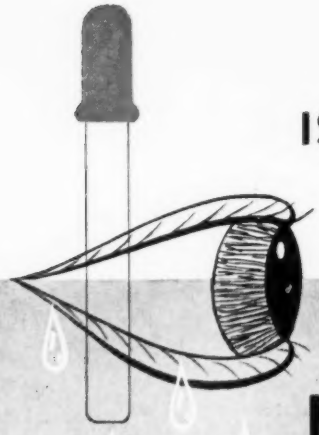

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